stryker

Adherus®

AutoSpray Dural Sealant

Instructions for Use

REF NUS-106
REF NUS-109
REF NUS-109-01

Legend

1 2 3	Used to refer to a graphic.
▶	Used for an instructional step that must be performed.
1. 2. 3.	Used for instructional steps that must be performed in a sequence.
•	Used for unordered list items.
Italic	Used for references and for table or figure titles.
🛈	Used to supplement or clarify information.
⚠ WARNING	Indicates a hazardous situation that, if not avoided, could result in death or serious injury.
⚠ CAUTION	Indicates a hazardous situation that, if not avoided, could result in minor or moderate injury.
NOTICE	Indicates information that is considered important, but not hazard-related, for example messages relating to property damage.

Table of contents

1 Introduction

1.1 About this document

This document pertains to the Adherus AutoSpray Dural Sealant and Adherus AutoSpray ET Dural Sealant products (Adherus AutoSpray Dural Sealant). For further information, refer to *Section 3.1 "Product overview."*
This document is the most comprehensive source of information for the safe and effective use of the product. Read this document carefully and pay attention to safety information. Keep this document accessible to users.

1.2 Other applicable documents

For further information on Stryker's electronic instructions for use (eIFU), go to ifu.stryker.com. For additional information, refer to product catalogs, contact your Stryker sales representative, or contact Stryker customer service.

1.3 Definitions of terms, abbreviations, and symbols

The following table provides definitions of the terms used in this document.

Definitions of terms

Term	Definition
Healthcare professional	A healthcare professional is a surgeon, nurse, professional caregiver, or OR medical staff.
Sterile barrier	Minimum packaging that minimizes the risk of ingress of microorganisms and allows the aseptic presentation of the sterile contents at the point of use
Sterilization	Process used to render products free from viable microorganisms

The following table provides definitions of the abbreviations used in this document.

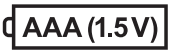
Definitions of abbreviations

Abbreviation	Definition
BCNU	Bis-chloroethylnitrosourea, carmustine
CISPR 11	Technical standard that covers radio-frequency disturbance characteristics for industrial, scientific, and medical equipment (limits and methods of measurement)
cm	Centimeter
CMF	Craniomaxillofacial
CMR	Carcinogenic, mutagenic, or toxic to reproduction
CSF	Cerebrospinal fluid
CW	Continuous wave
eIFU	Electronic instructions for use
ESD	Electrostatic discharge
ET	Extended tip
HCP	Healthcare professional
IEC	International Electrotechnical Commission
IFU	Instructions for use
ITT	Intent to treat
LTFU	Lost to follow-up
MR	Magnetic resonance
MRI	Magnetic resonance imaging
OR	Operating room
PEI	Polyethyleneimine
PEG	Polyethylene glycol
REF	Catalog number
RF	Radio frequency
% w/w	Percent weight-by-weight: To express the concentration of a solution

The following table provides the symbols used in this document, on the product, and on the product label.

Definitions of symbols

Symbol	Definition
	General warning sign: to signify a general warning.
	It is used to supplement or clarify information.
	Manufacturer: indicates the medical device manufacturer.
	Date of manufacture: indicates the date when the medical device was manufactured.
	Use-by date: indicates the date after which the medical device is not to be used.
	Batch code: indicates the manufacturer's batch code so that the batch or lot can be identified.
	Catalog number: indicates the manufacturer's catalog number so that the medical device can be identified.
	Sterilized using irradiation: indicates a medical device that has been sterilized using irradiation.
	Do not resterilize: indicates a medical device that is not to be resterilized.
	Do not use if package is damaged: indicates a medical device that should not be used if the package has been damaged or opened.
	Keep away from sunlight: indicates a medical device that needs protection from light sources.
	Temperature limit: indicates the temperature limits to which the medical device can be safely exposed.
	Humidity limitation: indicates the range of humidity to which the medical device can be safely exposed.
	Atmospheric pressure limit: indicates the range of atmospheric pressure to which the medical device can be safely exposed.

Symbol	Definition
	Do not reuse: indicates a medical device that is intended for one use, or for use on a single patient during a single procedure.
	Consult instructions for use: indicates the need for the user to consult the instructions for use.
	Direct current: to indicate on the rating plate that the equipment is suitable for direct current only; to identify relevant terminals.
	Designated End Equipment Type: Type BF applied part: to identify a type BF applied part complying with IEC 60601-1.
	"ON"/"OFF" (push-push): to indicate connection to or disconnection from the mains, at least for main switches or their positions, and all those cases where safety is involved. Each position, "ON" or "OFF," is a stable position.
	Quantity: indicates the number of medical devices in the packaging.
GTIN	Global Trade Item Number
	Single sterile barrier system
	Unique Device Identifier: indicates a carrier that contains Unique Device Identifier information
UDI-DI	Unique device identification
	Indicates that the product must be collected separately and must not be disposed of as unsorted municipal waste.
Rx Only	Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.
	Biological hazard (virus or toxin)
	To indicate generally elevated, potentially hazardous, levels of non-ionizing radiation, or to indicate equipment or systems, e.g., in the medical electrical area that include RF transmitters or that intentionally apply RF electromagnetic energy for diagnosis or treatment
	AAA (1.5 V) battery

2 Safety information

This section presents general product-related safety information and recommendations for the safe and effective use of the product. For specific safety information, instructions, and recommendations, refer to each section.

If a product-related incident occurs, report the incident to both the manufacturer and the national competent authority where the user or patient is established.

2.1 Warnings

Careless handling

Careless handling or storage of products may result in loose parts, lost products, or damage to products. This may lead to patient harm.

- Keep out of sunlight.
- Do not use if the PEG ester powder is not free-flowing.
- If the product is damaged, then dispose of the product.
- Use products for their intended use only.
- Do not remove any device covers except for the battery cover.

Product modification

Modifying the product may result in product damage. This may lead to patient harm.

- Do not modify the product or any accessories except as directed or intended by the instructions for use.

Implantation of a non-implant

Implantation of materials that are not intended as implants may lead to patient harm.

- Ensure all materials that are not specifically intended as implants are removed from the patient before surgical completion.

Single-use products

This single-use product must not be reused, as the single-use product is not designed to perform as intended after the first usage. Changes in mechanical, physical, or chemical characteristics caused by repeated use, cleaning, and resterilization may compromise the integrity of the design or materials leading to diminished safety, performance, or compliance with applicable specifications.

- Use a single-use product only once.
- Dispose of a used single-use product properly.

Damaged packaging

Damaged or open packaging, flaws in the sterile barrier, or an expired shelf life are indicators of possible product contamination.

- If a product has damaged or open packaging or flaws in the sterile barrier, dispose of the product.
- If the shelf life of a product is expired, dispose of the product.

2.2 Caution

Disposal

Incorrect disposal of a product may lead to healthcare professional harm or to environmental damage. This may result in the spread of bloodborne pathogens.

- Dispose of products in accordance with local regulations.
- Pay attention to the sharp edges of products to prevent injuries and cross-contamination.
- Dispose of sharp products and empty glass items in a sharps container.

3 Product information

This section provides product information of the Adherus AutoSpray Dural Sealant. For further details on the proper use of the product during surgery, refer to *Section 4 "Usage instructions."*

The product is supplied sterile. Sterile products are marked with the word STERILE.

3.1 Product overview

For further details about the correct use of the product during surgery, refer to *Section 4.2 "Intraoperative use."*

3.1.1 Product reference numbers

REF NUS-106	Adherus AutoSpray Dural Sealant (case of 5)
REF NUS-109	Adherus AutoSpray ET Dural Sealant (case of 5)
REF NUS-109-01	Adherus AutoSpray ET Dural Sealant Single Pack

3.1.2 How the device works

The product is provided with a ready-to-use applicator and 2 glass vials.

The applicator contains buffer solutions in both syringes.

The vials contain the following:

- Activated PEG ester powder
- PEI dissolved in sterile water

The pump within the applicator generates an air flow to aid in the delivery of the sealant from the nozzle onto the target site to be covered. The sealant cross-links and covers the target site to provide watertight closure.

The sealant application can be interrupted during the procedure: The nozzle will not clog if the pump remains active.

The sealant is an implantable medical device and absorbed by the body in approximately 90 days. During this time, healing may progress.

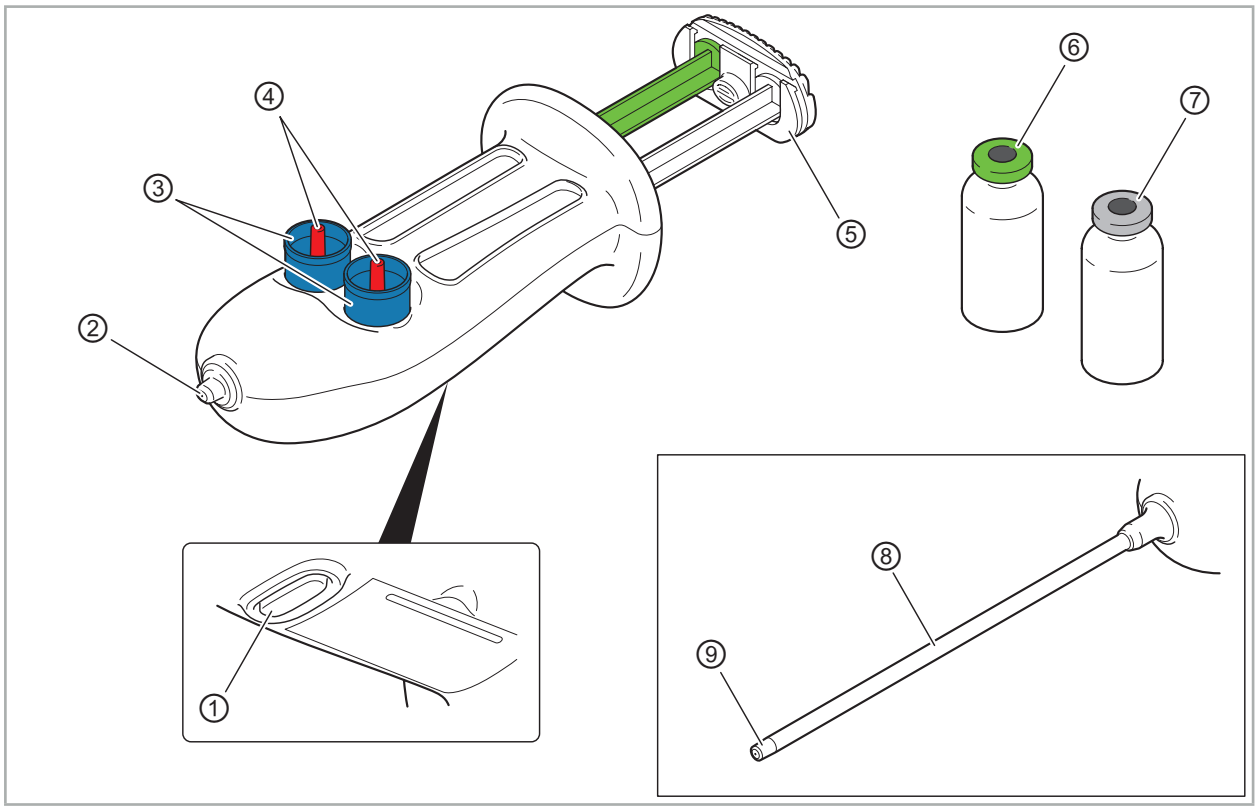
3.1.3 Operating mode and maintenance

The Adherus AutoSpray Dural Sealant is a sterile, single-use, electromechanical, battery-powered, non-repairable device.

The product does not require on-site maintenance or installation to ensure basic safety and electromagnetic compatibility. The product is not connected to a power source, so there is no need for shielding or grounding maintenance.

3.1.4 Product components

The Adherus AutoSpray Dural Sealant consists of the following components:



1. On/off button
2. Nozzle applicable to NUS-106 (applied part that may touch the body of the patient)
3. Vial adapter hub
4. Caps (to be removed)
5. Syringe plunger
6. Green capped vial with PEG ester powder
7. Silver capped vial with PEI solution
8. Nozzle applicable to NUS-109 (applied part that may touch the body of the patient)
9. Extended tip (not removable) applicable to NUS-109

Graphic 1: Applicator features

3.2 Intended use

Adherus AutoSpray Dural Sealant and Adherus AutoSpray ET Dural Sealant are intended for use as an adjunct to standard methods of dural repair, such as sutures, to provide watertight closure during cranial and spinal procedures.

3.3 Indications for use

Adherus AutoSpray Dural Sealant and Adherus AutoSpray ET Dural Sealant are indicated for use in patients who are 13 years of age and older, as an adjunct to standard methods of dural repair, such as sutures, to provide watertight closure during cranial and spinal procedures.

3.4 Contraindications

The Adherus AutoSpray Dural Sealant and Adherus AutoSpray ET Dural Sealant devices should not be used in confined anatomical spaces where nerve compression is of concern. The hydrogel may swell by up to 13 % of its size in any dimension or 46 % by volume after application.

3.5 Intended patient population

The Adherus AutoSpray Dural Sealant and Adherus AutoSpray ET Dural Sealant devices are intended to be used on patients ≥ 13 years undergoing surgical procedures and requiring dural repair. Dural defects can be induced by durotomy or dural tear.

3.6 Adverse effects

Adverse effects are potentially unwanted harmful effects associated with the use of the product or the surgical procedure.

Adverse effects associated with the use of the product may include:

- CSF leak including pseudomeningocele
- Adverse surgical site reactions, e.g., infection, meningitis, inflammation, edema
- Neurological complications, e.g., convulsion, dysphagia, meningitis, neurological deficits
- Surgical trauma resulting in hematoma
- Immunological reactions, e.g., allergic reaction, swelling of the face
- Hydrogel swelling resulting in nerve compression

Potential adverse effects associated with the surgical procedure or underlying condition include:

- Allergic reaction
- Blood and lymphatic system disorders
- Cardiac disorders
- Dermatologic events
- Gastrointestinal disorders
  - Nausea and/or vomiting
- General disorders
  - Delayed healing
  - Wound dehiscence
  - Chronic pain
- Hematologic abnormality
- Infections and infestations
  - Deep incisional surgical site infections
  - Superficial surgical site infections
  - Meningitis (aseptic or bacterial)
  - Encephalitis
  - Late incisional surgical site infections
- Inflammatory reaction
  - Arachnoiditis
- Musculoskeletal events
- Neoplasms benign and malignant, including cysts and polyps
- Nervous system disorders
  - Acute gait dysfunction
  - Chronic subdural hematoma and effusion
  - Dural-cutaneous fistula
  - Epidural hematoma
  - Headache
  - Seizure
  - Cerebral hemorrhage
  - CSF leak
  - Double vision
  - Hydrocephalus

  - Cerebral edema
  - Brain tumor
  - Severe neurological deficit post-op
  - Respiratory and thoracic disorders
  - Leakage of cerebrospinal fluid
  - Pseudomeningocele
  - Pneumocephalus
  - Spinal abscesses
- Renal compromise

For the specific adverse events that occurred in the clinical study, refer to *Section 3.10 "Clinical information."*

3.7 Clinical benefit

The Adherus AutoSpray Dural Sealant and Adherus AutoSpray ET Dural Sealant provide watertight closure during dural repair, and are designed to reduce the risk of CSF leak occurrences in the postoperative phase.

3.8 Intended users

These products are intended for use only by an educated HCP. The HCP must be licensed to perform surgery in the respective field of medicine and be familiar with the principles of surgical procedure. The HCP must prepare the products according to the procedure to be performed and must be familiar with the instructions for use in order to ensure proper operation and processing of this product.

The HCP performing any procedure is responsible for determining the appropriateness of using the product and the specific techniques to be used for each patient.

3.9 For use with

⚠ CAUTION

Unauthorized accessories or transducers may result in increased electromagnetic emissions or decreased electromagnetic immunity of this device. Improper operation of the device may lead to patient harm.

For further details, refer to *Section 4 "Usage instructions."*

3.10 Clinical information

3.10.1 Spinal clinical information

A prospective, randomized (1:1), controlled, single-blind, multicenter, pivotal clinical study was conducted to compare the safety and effectiveness of Adherus AutoSpray Dural Sealant with DuraSeal Exact Spine Sealant System when used in conjunction with standard methods of dural repair in spinal procedures.

Subjects were enrolled between January 19, 2021, and January 24, 2025. The database reflected data collected through August 29, 2025, and included 94 subjects. There were 14 investigational sites, all within the United States (US).

The study included an independent medical monitor responsible for review of safety-related events and an independent Clinical Events Committee (CEC) to adjudicate adverse events regarding severity and relatedness to the device and procedure.

Key inclusion/exclusion criteria for the study included the following:

Pre-operative inclusion criteria:

Enrolled subjects met the following inclusion criteria for enrollment; all criteria were answered "yes":

1. Subject is ≥ 18 and ≤ 75 years old.
2. Subject is scheduled for an elective spinal procedure that will require a planned durotomy.
3. Subject requires a procedure involving a Class I/clean wound (uninfected surgical wound in which no inflammation is encountered).
4. Subject is able and willing to provide informed consent and Health Insurance Portability and Accountability Act (HIPAA) authorization.
5. Subject is able and willing to meet all study requirements, including attending all post-index procedure assessment visits and radiological tests.

Intraoperative inclusion criteria:

6. Subject has durotomy edges that can be re-approximated using the investigator's standard methods of dural repair.

Pre-operative exclusion criteria:

Enrolled subjects did not meet any of the following exclusion criteria; all criteria were answered "no":

1. Subject has clinically significant hydrocephalus or clinical evidence of altered CSF dynamics.
2. Subject has a pre-existing external lumbar CSF drain or internal CSF shunt.
3. Subject has experienced previous CSF leak (secondary to trauma, neoplasm, surgery or other etiology).
4. Subject is undergoing a Chiari malformation procedure.

5. Subject has undergone a previous spinal procedure in the same anatomical location.
6. Subject has had radiation treatment to the surgical site, or standard fractionated radiation therapy is planned within 10 days post index-procedure.
7. Subject has spinal metallic implants that may cause significant imaging artifact on the magnetic resonance imaging (MRI) evaluation of the spine.
8. Subject has metallic implant(s) that are not compatible with [(MRI), e.g., cochlear implant, neurostimulator, stent, surgical clip, cardiac pacemakers, or other non-MRI compatible implants], or an elective implant of such devices is planned during the course of the study. Note: mercury amalgam dental fillings or similar metallic dental prostheses are not an exclusion criterion.
9. Subject has a known malignancy or another condition with anticipated survival shorter than six months.
10. Subject has undergone chemotherapy treatment, excluding hormonal therapy, within three weeks prior to the planned index procedure, or chemotherapy treatment is planned within two weeks after the index procedure is performed.
11. Subject has been treated with chronic steroid therapy (defined as regular (daily) administration of steroid agent(s) for ≥ 8 weeks) unless discontinued greater than four weeks prior to the planned index procedure. Note: standard acute perioperative steroids are permitted; administration of steroid agents for < 8 weeks duration prior to the planned index procedure is permitted.
12. Subject has received warfarin, heparin, other anticoagulant agents, aspirin or non-steroid anti-inflammatory agents on a daily basis and pre-surgical, standard of care drug wash-out did not occur.
13. Subject has a compromised immune system or autoimmune disease or is on chronic immunosuppressant agents at baseline.
14. Subject has a systemic infection or evidence of any infection near planned operative site.
15. Subject has a serum creatinine level > 2.0 mg/dL.
16. Subject has a serum total bilirubin > 2.5 mg/dL at baseline.
17. Subject has uncontrolled diabetes as evidenced by an HbA1c > 7 % prior to surgery.
18. Subject has a known allergy to FD&C Blue #1 and/or FD&C Yellow #5 or any of the constituents of the dural sealants.
19. Subject is pregnant, breast-feeding, or intends to become pregnant during the course of the study.
20. Subject is participating in a clinical trial of another investigational drug or device and has not completed the required follow-up period.

Intraoperative exclusion criteria

1. Subject has an incidental finding that meets any pre-operative exclusion criterion listed above.
2. Subject's dural defect cannot be closed with suture and/or duraplasty material.
3. Subject has a gap > 2 mm present between dural edges, or between the edge of dura and duraplasty material, based on visual estimate by surgeon before application of the surgical sealant.
4. Subject had undergone laminoplasty decompression.
5. Subject had undergone a syringomyelia procedure where the shunt is not placed in the subarachnoid position.

Follow-up schedule

All subjects were scheduled to return for follow-up examinations at postoperative days 1-3 or hospital discharge (whichever occurred first), 30 days, and 90 days post-index procedure.

Pre-operative, intraoperative, and postoperative assessments included physical and neurological examinations, imaging (magnetic resonance imaging (MRI) and/or computed tomography imaging (CT)), laboratory measures, assessment for CSF leak and pseudomeningocele, and assessment of adverse events.

Clinical endpoints

The primary endpoint was the success rate defined as freedom from the following events:

- CSF leak or pseudomeningocele diagnosed by physical examination, biochemical assay or imaging through 90-day following the index procedure.
- Unplanned retreatment of the original surgical site, adjudicated as device-related by the CEC, other than CSF leak or pseudomeningocele formation or those related to the subject's pre-existing condition, through 90-day following the index procedure including:
  - treatment for deep infection
  - treatment for meningitis
  - minimally invasive procedures or return to the operating room for neurosurgical complications

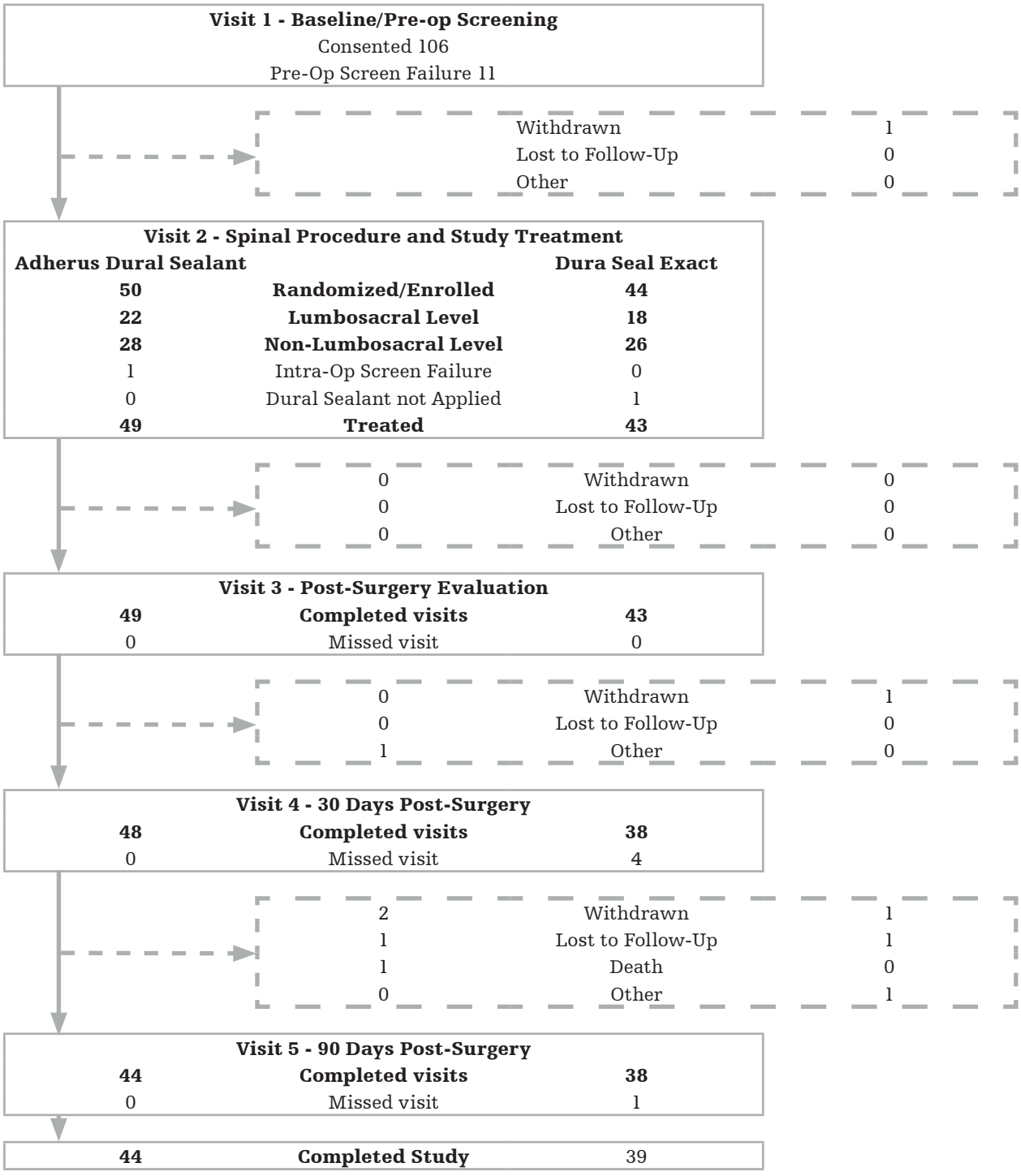
The primary endpoint was evaluated as a non-inferiority analysis with a non-inferiority margin (NIM) of 13.0 %. With regard to success/failure criteria, the study was considered a success if the null hypothesis was rejected at a one-sided 0.05 significance level demonstrating non-inferiority of the Adherus AutoSpray Dural Sealant to the DuraSeal Exact Spine Sealant System when considering the primary endpoint.

Subject accountability

At the time of database lock, of the 94 subjects enrolled in the study, 82 (87.2 %) subjects (44 in the Adherus AutoSpray Dural Sealant (test) group and 38 in the DuraSeal Exact Spine Sealant System (control) group had data available for analysis at the 90-day postoperative visit. A total of four subjects withdrew from the study prior to the 90-day endpoint, two in each of the test and control groups. One test subject died prior to the 90-day follow-up.

Additionally, two patients were lost to follow-up, one in each group, and two subjects exited the study for other reasons. One subject in each of the test group and control group were excluded due to administrative error. The site of the test subject did not have appropriate documentation to quantify as officially lost to follow-up (LTFU)). One subject in the control arm missed the 90-day visit. The following figure presents subject disposition at each follow-up visit.

Subject disposition for spinal clinical study



The following analysis populations were defined in the protocol and the following table reports the number of subjects in each population.

Intent-to-Treat (ITT): This analysis population includes all randomized and will be analyzed per the assigned treatment, regardless of actual treatment received. The primary analysis will be conducted using the ITT population.

Per-Protocol (PP): This analysis population includes all subjects who receive the treatment to which they were randomized and without protocol deviations that could impact the study outcomes.

Number of subjects by analysis population

Study population	Test	Control	Total
Enrolled / Randomized	50	44	94
ITT (Intent to treat)	49	43	92
PP (Per protocol)	41	35	76
Completed	44	39	83

Summary of demographic information for spinal clinical study subjects

Characteristics	Test population	Control population
Number of subjects	50	44
Men/women	22/28	25/19
Median age (years)	54.1	61.6
Primary indication for surgery (N (%))		
Intradural Tumor	41/49 (83.7)	32/44 (72.7)
Intradural Lesion	5/49 (10.2)	6/44 (13.6)
Tethered Cord	0/49 (0.0)	1/44 (2.3)
Vascular Malformation	0/49 (0.0)	3/44 (6.8)
Arachnoid Cyst	2/49 (4.1)	1/44 (2.3)
Syringomyelia	0/49 (0.0)	0/44 (0.0)
Other	1/49 (2.0)	1/44 (2.3)
Anatomical location (N (%))		
Lumbar or Lumbosacral	21 (42.9)	18 (41.9)
Cervical or Thoracic	28 (57.1)	25 (58.1)
Approach (N (%))		
Anterior	1 (2.0)	1 (2.3)
Dorsal	40 (80.0)	36 (81.8)
Lateral	0 (0.0)	0 (0.0)
Other	9 (18.0)	7 (15.9)

Characteristics	Test population	Control population
Primary technique for dural closure (N (%))		
Suture	36 (73.5)	31 (70.5)
Suture + autologous dural material	0 (0.0)	1 (2.3)
Suture + non-autologous dural material	12 (24.5)	11 (25.0)
Other	1 (2.0)	1 (2.3)

Study results

Primary endpoint analysis

The primary composite endpoint analysis was defined as freedom from CSF leak or pseudomeningocele and freedom from unplanned retreatment of the original surgical site through 90 days post index procedure.

The primary composite endpoint rate was 93.9 % for the test group and 91.8 % for the control group based on the ITT population and using multiple imputation to impute missing data as shown in the table below. Since the lower bound of the 90 % confidence interval for the difference in the primary endpoint event rate was < 13 %, the non-inferiority endpoint was met (p = 0.004). Component level data for the primary endpoint is also shown in the table below indicating that treatment groups generally performed similarly when considering each component.

A supportive analysis using observed data, excluding missing data rather than using multiple imputation, resulted in a primary endpoint analysis of 95.5 % (42/44) for the test group and 92.1 % (35/38) for the control group. Component level data for the primary endpoint, excluding missing data rather than using multiple imputation, resulted in an overall success rate of 97.7 % (43/44) for the test group and 92.1 % (35/38) for the control group for freedom from CSF leak or pseudomeningocele and an overall success rate of 97.7 % (43/44) for the test group and 100 % (38/38) for the control group for freedom from unplanned retreatment of the original surgical site. These results are similar to those observed for the primary analysis population and a sensitivity analysis on the PP population (94.7 % (36/38) test group and 90.9 % (30/33) control group), suggesting robustness of the study conclusions.

A tipping point analysis was also conducted to evaluate the impact of missing data on the primary endpoint conclusion across all possible missing data scenarios. The results of the tipping point analysis did not indicate missing data largely impacted study outcomes, further supporting robustness of the study conclusions.

Primary composite endpoint results and component-level outcomes (ITT)

Primary composite endpoint	Test group (N = 49)	Control group (N = 43)	Difference (test - control)
Composite endpoint outcome			
Primary composite endpoint success through 90 days post index procedure[1], *	93.9 % (86.8 %, 100.0 %)[2]	91.8 % (83.0 %, 100.0 %)[2]	2.2 % (−7.2 %, 11.5 %)[3]
P-Value (H0: $\pi_A \leq \pi_D - 13$ %)	--	--	0.004
Component level outcomes			
Freedom from CSF leak or pseudomeningocele through 90 days post index procedure[4, *]	96.5 % (90.8 %, 100.0 %)[2]	91.1 % (82.0 %, 100.0 %)[2]	5.4 % (−3.6 %, 14.4 %)[3]
Freedom from unplanned retreatment of the original surgical site through 90 days post index procedure[5, *]	97.3 % (92.2 %, 100.0 %)[2]	99.8 % (97.8 %, 100.0 %)[2]	-2.5 % (−7.1 %, 2.1 %)[3]

* For the primary analysis, subjects that were not assessed for adverse events at the 90-day follow-up visit and did not experience a qualifying CSF leak, pseudomeningocele, or unplanned retreatment of the original surgical site (all as defined above) through 90 days post index procedure had their outcome determined using multiple imputation.

1 A subject is considered a primary composite endpoint success if they are free from CSF leak and pseudomeningocele and free from unplanned retreatment of the original surgical site (all as defined above) through 90 days post index procedure.
2 Two-sided 95 % Confidence interval
3 Two-sided 90 % Confidence interval
4 CSF leak and pseudomeningocele as adjudicated by the CEC.
5 Unplanned retreatment of the original surgical site only includes those adjudicated by the CEC as being for a reason other than CSF leak or pseudomeningocele, as being related to the device, and as being not related to pre-existing conditions.

Adverse events

The safety analysis was based on all adverse events (AEs) observed in all subjects enrolled in the study through the 90-day post-surgery evaluation. The key safety findings for this study are reported in the table below. Another table below provides a listing of all adverse events observed through 90 days.

The most commonly reported AEs were infection-related events which occurred in similar number between groups (4.0 % (2/50) test group and 6.8 % (3/44) control group). No deep infections, meningitis, or CSF leaks were reported in either group. There were no AEs due to device deficiencies/malfunctions or Unanticipated Adverse Device Effects (UADEs) in the study.

Serious adverse events (SAEs) occurred more frequently in the test group (20.0 %) compared to the control group (15.9 %). Twenty-two SAEs were reported across 10 test subjects (20.0 %), one was a superficial infection, one was a pseudomeningocele (2.0 %, 1/50), and the remaining 20 SAEs were other events (16.0 %, 8/50). Eighteen SAEs were reported in 7 (15.9 %) control subjects. Two of these were infections, with the remaining 16 classified as other events (15.9 %, 7/44). SAEs classified as “other” for the test group consisted of events that were neurological, orthopedic, oncological, cardiovascular, gastrointestinal, or urological in nature. SAEs classified as “other” for the control group consisted of the categories above as well as otolaryngolic, pulmonary, immunological, and hepatic.

Of the test AEs, six were possibly related to the study device seen in 3/50 subjects (6 %), and zero were definitely related to the device. The control group had three AEs that were possibly related to the device in 3/44 subjects (6.8 %) and one was definitely related in 1/44 subjects (2.3 %). No SAEs for either treatment group were considered definitely related to the device. Six and one SAEs were considered possibly related to the study device for the test and control devices, respectively.

Overall incidence of AEs by seriousness and relation through 90 days (all enrolled population)

Relatedness	Test group n/N (%)		Control group n/N (%)	
AE type	**Events**	**Subjects**	**Events**	**Subjects**
All AEs through 90 days	77	20/50 (40.0 %)	95	24/44 (54.5 %)
All SAEs through 90 days	22	10/50 (20.0 %)	18	7/44 (15.9 %)
All device related AEs[6]	6	3/50 (6 %)	4	4/44 (9.1 %)
All device related[6] SAEs	6	3/50 (6 %)	1	1/44 (2.3 %)
Death[7]	1	1/50 (4.0 %)	0	0/44 (0.0 %)
Infection	2	2/50 (4.0 %)	3	3/44 (6.8 %)
Superficial	1	1/50 (2.0 %)	1	1/44 (2.3 %)
Deep	0	0/50 (0.0 %)	0	0/44 (0.0 %)
Meningitis	0	0/50 (0.0 %)	0	0/44 (0.0 %)
other	1	1/50 (2.0 %)	2	2/44 (4.5 %)
CSF Leak	0	0/50 (0.0 %)	0	0/44 (0.0 %)
Pseudomeningocele	1	1/50 (2.0 %)	3	3/44 (6.8 %)
Retreatment of surgical site	0	0/50 (0.0 %)	0	0/44 (0.0 %)

AEs reported at a rate of greater than 1 % are summarized in the *Table "Summary of spinal clinical study adverse events through 90 days (ITT)."*

Summary of spinal clinical study adverse events through 90 days (ITT)

Adverse event	Test subjects (n (%)) N = 49	Control subjects (n (%)) N = 43
Lhermitte's syndrome	1 (2.0)	0 (0.0)
Weakness - upper extremity	2 (4.1)	2 (4.7)
Paresthesia - upper extremity	3 (6.1)	2 (4.7)
Pain - upper extremity	2 (4.1)	1 (2.3)
Swelling - upper body	1 (2.0)	4 (9.3)
Weakness - lower extremity	3 (6.1)	5 (11.6)
Paresthesia - lower extremity	3 (6.1)	4 (9.3)
Pain - lower extremity	4 (8.2)	0 (0.0)
Swelling - lower extremity	3 (6.1)	3 (7.0)

6 Device related AEs and SAEs are those that are possibly or definitely related to the device
7 Deaths were attributed to pre-existing oncological conditions

Adverse event	Test subjects (n (%)) N = 49	Control subjects (n (%)) N = 43
Weakness - back	3 (6.1)	0 (0.0)
Pain - back	3 (6.1)	8 (18.6)
Pain - chest	2 (4.1)	1 (2.3)
Pain - abdominal	4 (8.2)	2 (4.7)
Death (unrelated to product or procedure)	1 (2.0)	0 (0.0)
Neuropathy	2 (4.1)	0 (0.0)
Wound dehiscence	3 (6.1)	1 (2.3)
Dizziness	3 (6.1)	0 (0.0)
Headache	1 (2.0)	2 (4.7)
Seizure	1 (2.0)	0 (0.0)
Pulmonary embolism	2 (4.1)	0 (0.0)
Deep vein thrombosis	2 (4.1)	2 (4.7)
Pseudomeningocele	1 (2.0)	3 (7.0)
Urinary tract infection	4 (8.2)	2 (4.7)
Cancer recurrence	2 (4.1)	0 (0.0)
Covid-19	1 (2.0)	2 (4.7)
Hyperglycemia	1 (2.0)	2 (4.7)
Hypotension	1 (2.0)	1 (2.3)
Hip arthroplasty	1 (2.0)	0 (0.0)
Fever	1 (2.0)	1 (2.3)
Constipation	1 (2.0)	1 (2.3)
Incontinence	3 (6.1)	4 (9.3)
Dyspnea	1 (2.0)	2 (4.7)
Seroma	2 (4.1)	2 (4.7)
Leukocytosis	1 (2.0)	2 (4.7)
Traumatic foley placement	1 (2.0)	0 (0.0)

Adverse event	Test subjects (n (%)) N = 49	Control subjects (n (%)) N = 43
Oral thrush	1 (2.0)	0 (0.0)
Postural Orthostatic Tachycardia Syndrome (POTS)	1 (2.0)	0 (0.0)
Herniated disk	1 (2.0)	0 (0.0)
Atrial Fibrillation	0 (0.0)	1 (2.3)
Pain - neck	0 (0.0)	2 (4.7)
Tracheitis	0 (0.0)	1 (2.3)
Spinal cord compression	0 (0.0)	2 (4.7)
Inferior vena cava placement	0 (0.0)	1 (2.3)
Sepsis	0 (0.0)	2 (4.7)
Infection - systemic/pulmonary	0 (0.0)	3 (7.0)
Migraine	0 (0.0)	1 (2.3)
Arrhythmia	0 (0.0)	1 (2.3)
Urinary retention	0 (0.0)	1 (2.3)
Ileus	0 (0.0)	1 (2.3)
Anemia	0 (0.0)	1 (2.3)
Hypocalcemia	0 (0.0)	1 (2.3)
Hypomagnesemia	0 (0.0)	1 (2.3)
Hypokalemia	0 (0.0)	1 (2.3)
Epistaxis	0 (0.0)	1 (2.3)
Memory loss/confusion	0 (0.0)	2 (4.7)
Elevated hemidiaphragm	0 (0.0)	1 (2.3)
Cerumen impaction	0 (0.0)	1 (2.3)
Gastritis	0 (0.0)	1 (2.3)
Pleural effusion	0 (0.0)	1 (2.3)
Atelectasis	0 (0.0)	1 (2.3)
Tachycardia	0 (0.0)	1 (2.3)

Adverse event	Test subjects (n (%)) N = 49	Control subjects (n (%)) N = 43
Increased lactic acid	0 (0.0)	1 (2.3)
Hypoxemia	0 (0.0)	1 (2.3)
Adrenal insufficiency	0 (0.0)	1 (2.3)
Anemia	0 (0.0)	1 (2.3)
Spinal cord hemorrhage	0 (0.0)	1 (2.3)
Low sodium	0 (0.0)	1 (2.3)
Pedicle fracture	0 (0.0)	1 (2.3)

3.10.2 Cranial clinical information

A prospective, randomized, controlled, multicenter pivotal trial has been conducted to evaluate the use of Adherus Dural Sealant, delivered using the Adherus AutoSpray applicator, as an adjunct to standard methods of dural repair, such as sutures, to provide watertight closure during cranial surgery. The primary endpoint of this study was a composite evaluation of the safety and effectiveness of Adherus AutoSpray Dural Sealant (n = 124 subjects) when compared to an active control (n = 126 subjects). The endpoint results were based on the number of subjects who were free from intra-operative CSF leakage from dural repair after up to two applications of sealant during the Valsalva maneuver, CSF leak/pseudomeningocele during the 120-day follow-up period and unplanned retreatment of the original surgical site within 120 days post-surgery. The overall success rate for the complete case analysis was 91.2 % in the Adherus group compared to 90.6 % in the control group. Adherus was found to be non-inferior to the control with the non-inferiority margin of 10 % ($p = 0.005$). In the early post-surgical period when the sealants are expected to function, the overall success rate at the 14-day follow-up on subjects who completed the visit was 99.1 % in the Adherus group compared to 95.0 % in the control group. In addition, the overall success rate at the 45-day follow-up on subjects who completed the visit was 96.6 % in the Adherus group compared to 91.9 % in the control group. The freedom from primary endpoint failure analysis also showed that the primary endpoint failures in the control group tended to occur early in the follow-up period while a majority of Adherus endpoint failures were identified through protocol-required radiographic imaging at the 120-day follow-up visit.

Safety was assessed based on evaluation of wound healing, surgical site infections, meningitis, worsening Modified Rankin Score, surgical site swelling and adverse events through the 120 day follow-up period. One hundred (80.6 %) subjects in the Adherus group and 98 (77.8 %) subjects in the control group experienced at least one adverse event within the 120 day follow-up period. There were no unanticipated adverse device effects. Among the subjects treated with Adherus AutoSpray Dural Sealant, there were no device-related deep wound infections and no cases of meningitis. The type and rate of adverse events observed in this study are consistent with the complexity of the surgical procedure and the co-morbid condition of the treated subjects.

Key inclusion/exclusion criteria for the study included the following:

Pre-operative inclusion criteria:

- Subject was ≥ 18 and ≤ 75 years of age.
- Subject was scheduled for an elective cranial procedure involving a dural incision using any of the following surgical locations / approaches (or combination): frontal, temporal, occipital and parietal (i.e., supratentorial), and/or midline or lateral suboccipital (i.e., infratentorial).
- Subject required a procedure involving a Class I/clean wound (uninfected surgical wound in which no inflammation was encountered).

Pre-operative exclusion criteria:

- Subject required a procedure involving a translabyrinthine, transsphenoidal, transoral approach, or any procedure that penetrates the air sinus or mastoid air cells. Note: Superficial penetration of mastoid air cells was not an exclusion if cells were appropriately sealed (e.g., bone wax).
- Subject had a CSF shunt such as; ventriculo-peritoneal, ventriculo-pleural, ventriculoatrial or lumbo-peritoneal shunts.
- Subject had an external ventricular or lumbar CSF drain that must be left in place after surgery.
- Subject had clinically significant hydrocephalus or clinical evidence of altered CSF dynamics.
- Subject had undergone a previous intracranial neurosurgical procedure in the same anatomical location. (Note: stereotactic biopsy was not exclusionary).
- Subject experienced previous CSF leak (secondary to trauma, neoplasm, surgery or other etiology).
- Subject had radiation treatment to the surgical site, or standard fractionated radiation therapy was planned within ten days post index-procedure. (Note: stereotactic radiosurgery prior to the planned index procedure was not an exclusion criterion).
- Subject had experienced a traumatic injury to the head within 30 days prior to the planned index procedure resulting in basilar skull fracture or fractures involving the paranasal sinuses.
- Subject had a known malignancy or another condition with anticipated survival shorter than six months.
- Subject had undergone chemotherapy treatment, excluding hormonal therapy, within three weeks prior to the planned index procedure, or use of intracavitary chemotherapy wafer (BCNU) was planned, or chemotherapy treatment was planned within two weeks after the index procedure was performed.
- Standard use of peri-operative steroids (i.e., corticosteroids) was permitted. Chronic steroid use (defined as daily use of corticosteroids for >/= 8 weeks) for the purposes of reducing the side effects of chemotherapy and/or radiation therapy for cancer was not exclusionary unless the patient was deemed by the investigator to be suffering from steroid toxicity. Use of corticosteroids on a chronic basis (as defined previously) for purposes other than decreasing the symptoms of systemic chemotherapy was exclusionary unless those steroids were discontinued 4 weeks prior to the planned index procedure.
- Subject received warfarin, heparin, other anticoagulant agents, aspirin or non-steroid anti-inflammatory agents on a daily basis and pre-surgical, standard of care drug washout did not occur.
- Subject had a documented clinically significant coagulopathy with a PTT > 37 seconds, or INR > 1.3 INR units.
- Subject had a compromised immune system or autoimmune disease, or was on chronic immunosuppressant agents at baseline.
- Subject had a systemic infection or evidence of any infection near planned operative site.

- Subject had a serum creatinine level > 2.0 mg/dL.
- Subject had a serum total bilirubin > 2.5 mg/dL at baseline.
- Subject had uncontrolled diabetes as evidenced by the Institution's standard of care (HbA1c > 7 % , blood glucose, etc at baseline

Intraoperative inclusion criteria

- Subject's linear extent of durotomy was ≥ 2cm
- Subject's dural margins from the edges of bony defect were ≥ 3mm throughout
- Subject's CSF leak was present intra-operatively following completion of primary dural closure (with or without non-autologous duraplasty or autologous tissue), either spontaneously or upon Valsalva maneuver, at up to 20 cm H_2O for up to five (5) seconds.

Intraoperative exclusion criteria

- Subject had an incidental finding that met any pre-operative exclusion criterion listed above.
- Subject required the intra-operative placement of a CSF diversion device (e.g., ventricular catheter, subdural catheter, lumbar drain, or other device designed to externally evacuate CSF) that was left in place after the procedure. Note: Subgaleal drains used for acute postoperative management of the incision site were permitted.
- Subject had a gap > 2 mm present between dural edges, or between the edge of dura and duraplasty material, based on visual estimate by surgeon before application of the surgical sealant.

Summary of demographic information for cranial clinical study subjects

Characteristics	Test population	Control population
Number of subjects	124	126
Men/women	41/83	40/86
Median age (years)	54.2	51.1
Subject ASA score (N (%))		
I	2 (1.6)	8 (6.3)
II	47 (37.9)	50 (39.7)
III	69 (55.6)	62 (49.2)
IV	6 (4.8)	6 (4.8)
V	0 (0.0)	0 (0.0)

Characteristics	Test population	Control population
Primary indication for surgery (N (%))		
Tumor	56 (45.2)	53 (42.1)
Epilepsy	1 (0.8)	1 (0.8)
Nerve decompression	17 (13.7)	21 (16.7)
AVM	3 (2.4)	5 (4.0)
Aneurysm	28 (22.6)	26 (21.3)
Chiari malformation	17 (13.7)	18 (14.3)
Cyst	2 (1.6)	1 (0.8)
Other	0 (0.0)	1 (0.8)
Approach (N (%))		
Infratentorial	53 (42.7)	52 (41.3)
Supratentorial	71 (57.3)	74 (58.7)
Primary technique for dural closure (N (%))		
Suture	48 (38.7)	48 (38.1)
Suture + autologous dural material	29 (23.4)	34 (27.0)
Suture + non-autologous dural material	45 (36.3)	39 (31.0)

AEs reported at a rate of greater than 1 % are summarized in the *Table "Summary of Adherus AutoSpray Dural Sealant cranial clinical study adverse events."*

Summary of Adherus AutoSpray Dural Sealant cranial clinical study adverse events

Adverse event	Subjects (n (%)) N = 49
Anaemia	3 (2.4)
Leukocytosis	2 (1.6)
Deafness unilateral	2 (1.6)
Tinnitus	4 (3.2)
Diplopia	5 (4.0)
Eyelid Ptosis	2 (1.6)
Periorbital oedema	6 (4.8)
Vision blurred	7 (5.6)
Dysphagia	4 (3.2)
Nausea	2 (1.6)
Adverse reaction	6 (4.8)
Chest pain	3 (2.4)
Disease progression	3 (2.4)
Death	4 (3.2)
Fatigue	2 (1.6)
Pneumonia	2 (1.6)
Urinary tract infection	2 (1.6)
Wound infection	2 (1.6)
Incision site hypoaesthesia	3 (2.4)
Incision site pain	4 (3.2)
Periorbital haemorrhage	3 (2.4)
Post procedural oedema	2 (1.6)
Pseudomeningocele	9 (7.3)
Seroma	3 (2.4)
Subdural haematoma	3 (2.4)
Wound dehiscence	2 (1.6)
Muscular weakness	2 (1.6)

Adverse event	Subjects (n (%)) N = 49
Aphasia	4 (3.2)
Balance disorder	2 (1.6)
Convulsion	5 (4.0)
Cranial nerve palsies multiple	2 (1.6)
Dizziness	7 (5.6)
Embolic stroke	2 (1.6)
Headache	14 (11.3)
Hemiparesis	2 (1.6)
Hypoaesthesia	4 (3.2)
Hypoglossal nerve paralysis	2 (1.6)
Memory Impairment	2 (1.6)
Nystagmus	3 (2.4)
Paraesthesia	5 (4.0)
Sensory loss	3 (2.4)
Tremor	2 (1.6)
VIIth nerve paralysis	3 (2.4)
Vocal cord paralysis	2 (1.6)
Atelectasis	2 (1.6)
Respiratory failure	2 (1.6)
Alopecia	2 (1.6)
Rash	2 (1.6)
Swelling face	4 (3.2)

4 Usage instructions

4.1 Before use

This section provides step-by-step instructions, safety information, and recommendations for the safe and effective use of the product before intra-operative use.

⚠ WARNING

If the required components for surgery are not available, not functional, or non-sterile, this may result in patient harm.

- ▶ Before use, ensure that all components that are needed for the operation are available and checked before use in the sterile surgical field.
- ▶ Do not use non-sterile products.

4.1.1 Medical research status

Adherus AutoSpray Dural Sealant has not been studied in:

- Patients requiring a procedure with a translabyrinthine, transsphenoidal, or transoral approach, or any procedure that penetrates the paranasal sinuses or mastoid air cells
- Patients with dural edge gaps larger than 2 mm
- Patients with severely impaired renal or hepatic function
- Patients with an active infection present at the surgical site
- Patients with treated or untreated hydrocephalus (e.g., those with CSF drainage devices or altered CSF dynamics)
- Patients with an underlying medical co-morbidity or taking a medication known to interfere with wound healing (e.g., those with previous intracranial neurosurgery or spinal surgery at the same anatomic site, radiation and chemotherapy treatment, known malignancy, diabetes, steroid toxicity and chronic corticosteroid use, compromised immune system, or taking an anticoagulant agent, aspirin or non-steroidal anti-inflammatory drug)
- Patients with a known allergy to FD&C blue #1 or FD&C yellow #5 dye
- Patients who are pregnant or lactating or intend to become pregnant during the course of treatment

4.1.2 Patient information

The surgeon must evaluate the possibility of subsequent clinical failure and discuss the following with the patient or their guardian:

- The expected surgery outcome
- The inherent limitations of the product
- Any postoperative physical limitations

⚠ WARNING

The patient or their guardian must be informed about the surgery and postoperative care instructions to ensure adequate healing and prevent product failures that may lead to patient harm.

▶ Inform the patient or their guardian regarding:
  - The expected surgery outcome and any postoperative physical limitations.
  - The potential adverse effects, refer to *Section 3.6 "Adverse effects."*

▶ Advise the patient or their guardian to:
  - Attend postoperative follow-up visits and medical check-ups.
  - Report any unusual changes in the operated site to their surgeon.

4.2 Intraoperative use

This section provides step-by-step instructions, safety information, and recommendations for the safe and effective use of the product during surgery.

⚠ WARNING

Use of the Adherus AutoSpray Dural Sealant device adjacent to other equipment should be avoided because it could result in improper operation.

▶ If such use is necessary, observe the Adherus AutoSpray Dural Sealant device and the other equipment to verify that they are operating normally.

When tested 8 hours after reconstitution, the sealant swelled slightly but statistically significantly more than samples reconstituted 1, 2, or 4 hours.

▶ Use the sealant within 2 hours of reconstitution of the crosslinking components.

The product is designed to be used in the limited environment of an OR.

▶ Do not use the product in the presence of flammable anesthetics, flammable anesthetics with oxidizing agents, or in an oxygen-rich environment.

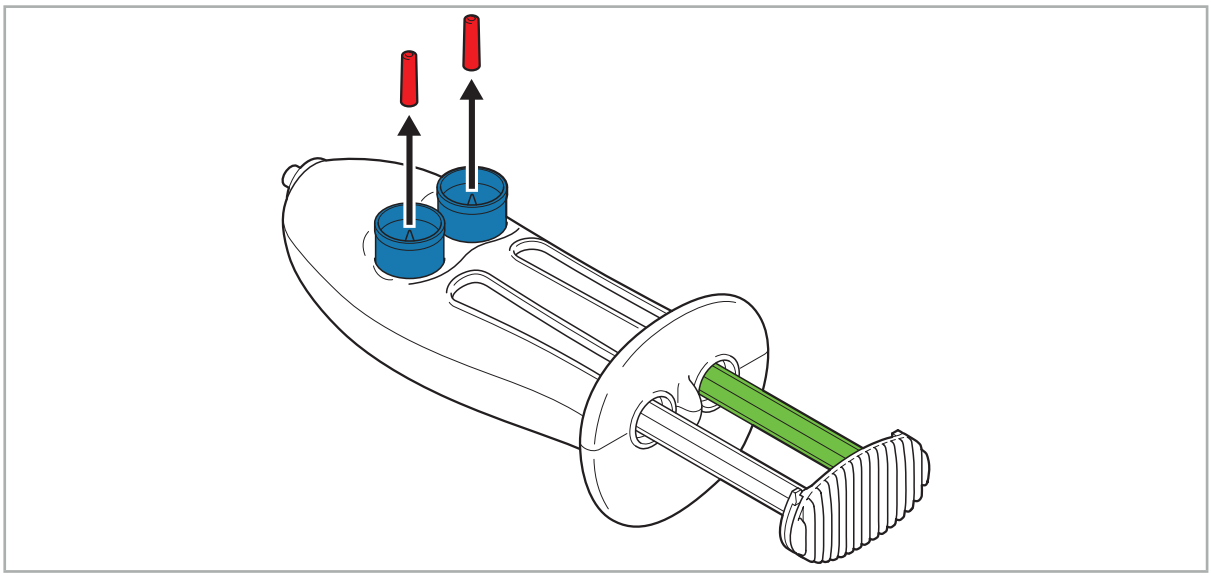
ⓘ The service life of the applicator battery is approx. 2 hours of continuous use.

4.2.1 Reconstituting the crosslinking components

Step-by-step instructions:

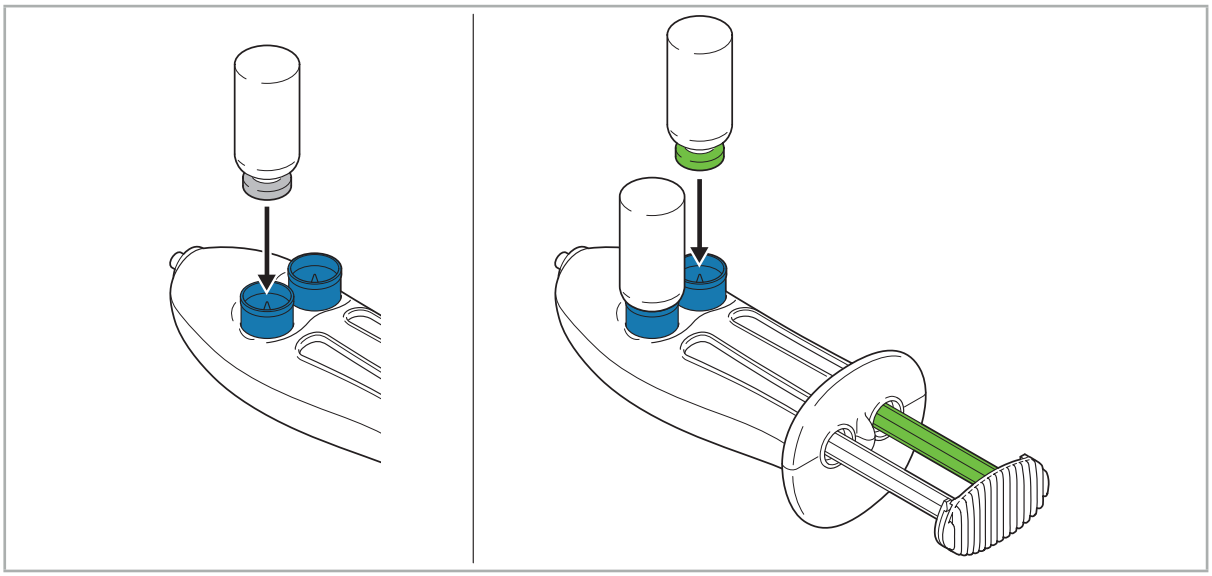
1. Place the package in the sterile area under aseptic conditions.
2. Remove the applicator and vials from the package.
3. Hold the applicator with the nozzle pointing upwards.
4. Remove the red caps that cover the vial adapter hubs and discard them.
   - If necessary, use a twisting motion and a tool such as a hemostat.

   Graphics show the applicator without an extended tip. They also apply to applicators with an extended tip.



Graphic 2: Removing the red caps

5. Holding the applicator firmly, push the silver end of the vial containing the PEI solution completely into the vial adapter hub of the white syringe plunger.
   - The spike of the vial adapter hub pierces through the septa.
   - The silver seal in the adapter attachment sits on the vial adapter hub. Refer to *Graphic 3*.
6. Holding the applicator firmly, push the green end of the vial containing the PEG ester powder completely into the vial adapter hub of the green syringe plunger.
   - The spike of the vial adapter hub pierces through the septa.
   - The green seal in the adapter attachment sits on the vial adapter hub.

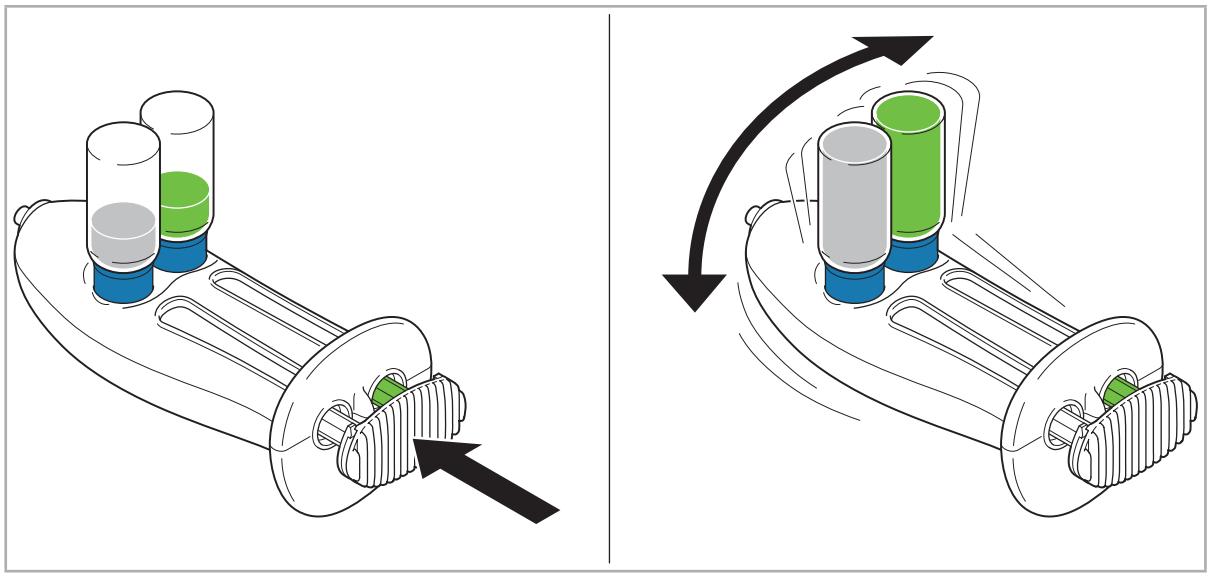


Graphic 3: Inserting the vials

7. With the vials facing upwards, press the syringe plunger.
   - Continue to press the syringe plunger until fully depressed.
   - If necessary, use 2 hands to operate the syringe plunger.
   - The liquids fill the vials.

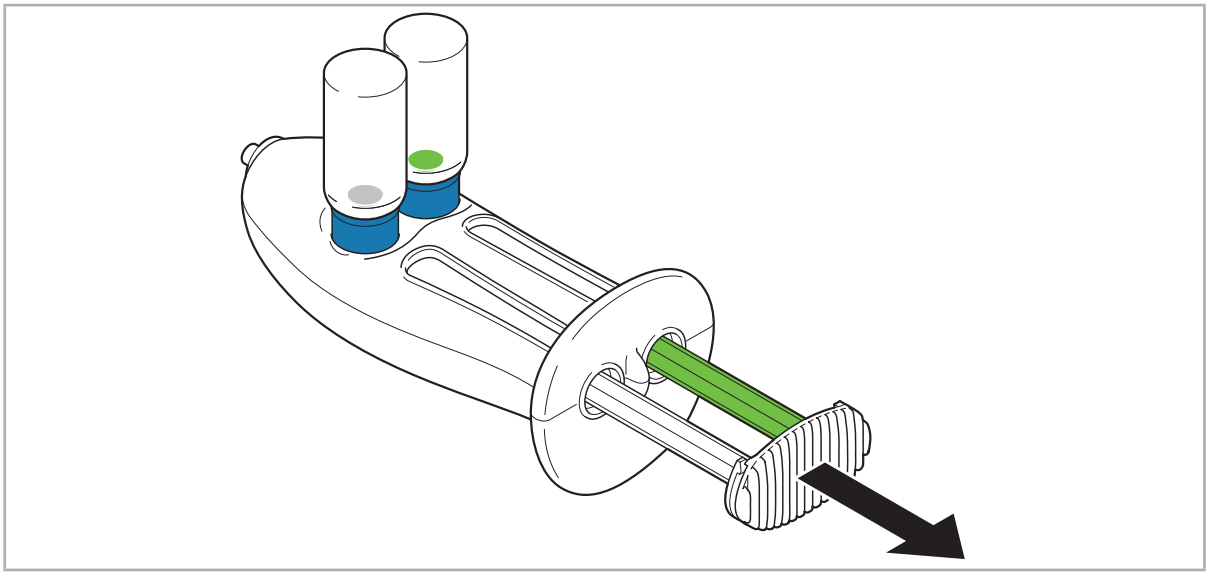
   ℹ The white and green plungers are interlocked to facilitate simultaneous pressing.

8. With the syringe plunger still depressed, shake the device until the powder is dissolved.
   - The PEG ester powder will continue to dissolve between shaking intervals.
   - Excessive shaking may result in excessive air bubble entrapment in the solution.



Graphic 4: Pressing the syringe plunger

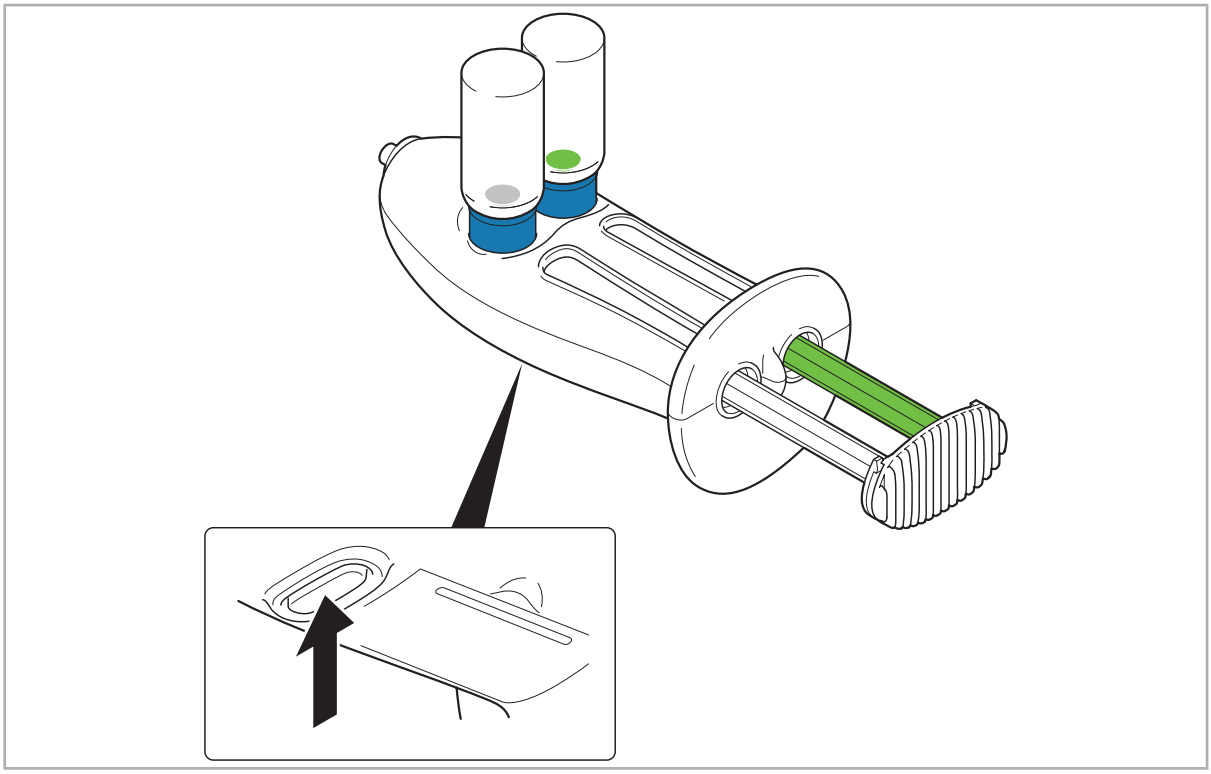
9. Release the syringe plunger and allow it to rebound.
10. Press the syringe plunger a second time so that both solutions are homogeneous.
11. Allow the syringe plunger to rebound.
12. Pull the syringe plunger backwards until all reconstituted components have been transferred from the vials.
    - If the on/off button is accidentally pressed during the reconstitution phase: Turn the applicator off. This will not affect the functionality of the applicator.



Graphic 5: Pulling the syringe plunger

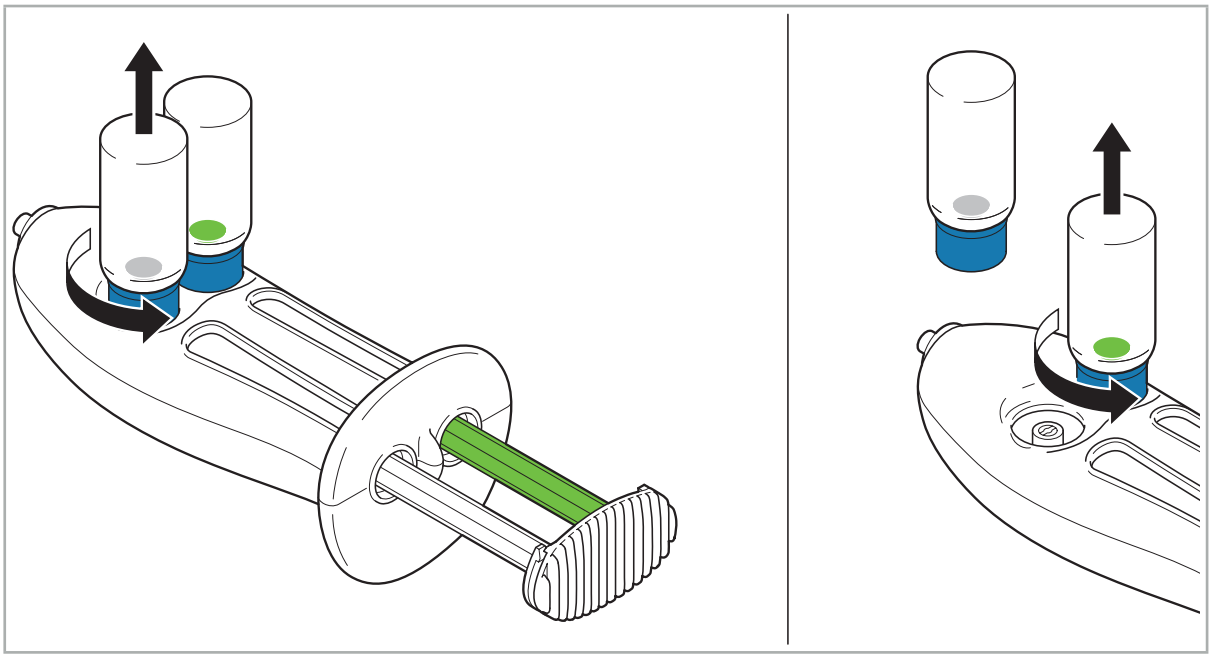
To achieve optimum results: Complete the application within 2 hours of reconstitution.

13. Press the on/off button on the underside to switch on the applicator. Refer to *Graphic 6*.
    - To prevent the nozzle from inadvertently clogging: Always switch on the applicator before removing the hubs of the vial adapter.
    - Do not use the applicator until a buzzing sound is audible.
    - If there is no sound from the applicator air pump: Follow the instructions in *Table "6 Troubleshooting."*
    - If troubleshooting is not successful: Use a new applicator.



Graphic 6: Pressing the on/off button

14. Orient the applicator so that the vials are facing upwards.
15. Remove both vial adapter hubs from the applicator.
    - Rotate the vial adapter hubs, including the vials, counterclockwise until they are ejected from the device.



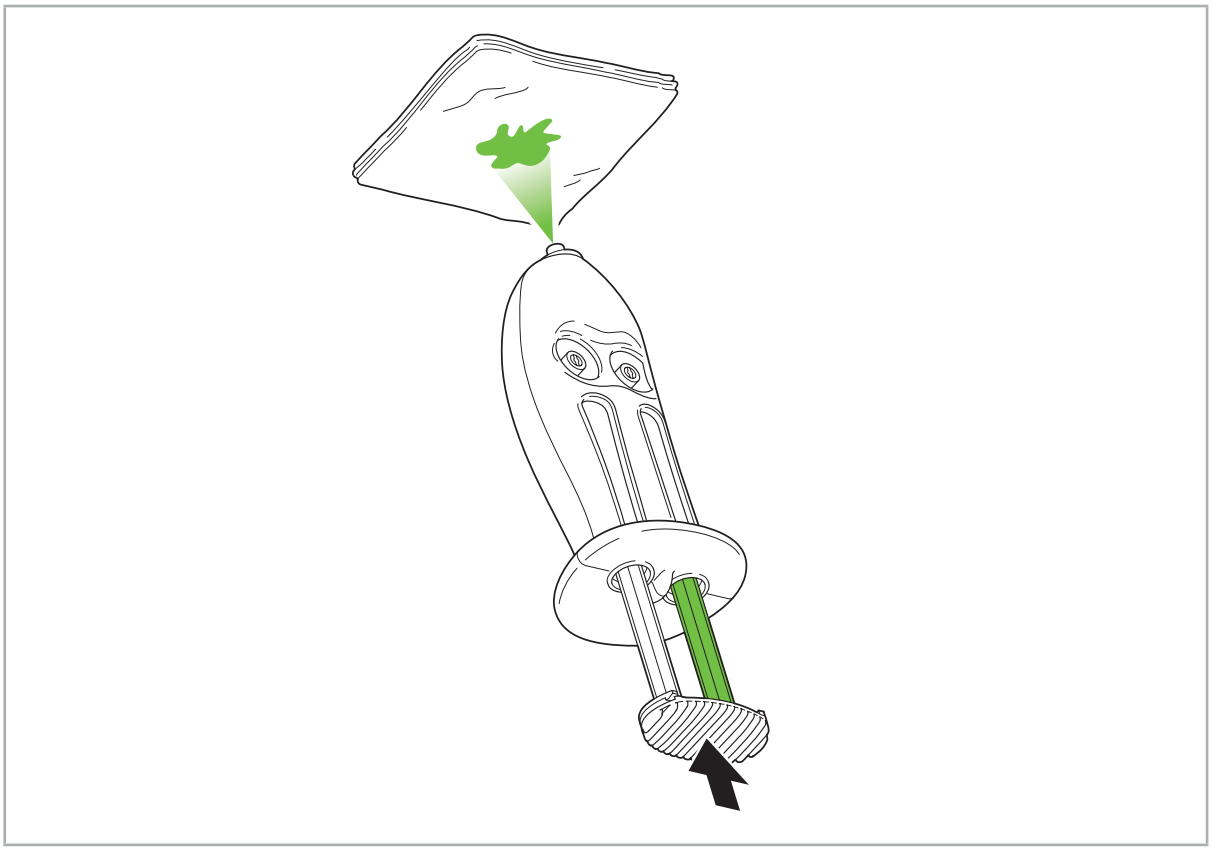
Graphic 7: Removing both vial adapter hubs

4.2.2 Applying the sealant

Step-by-step instructions:

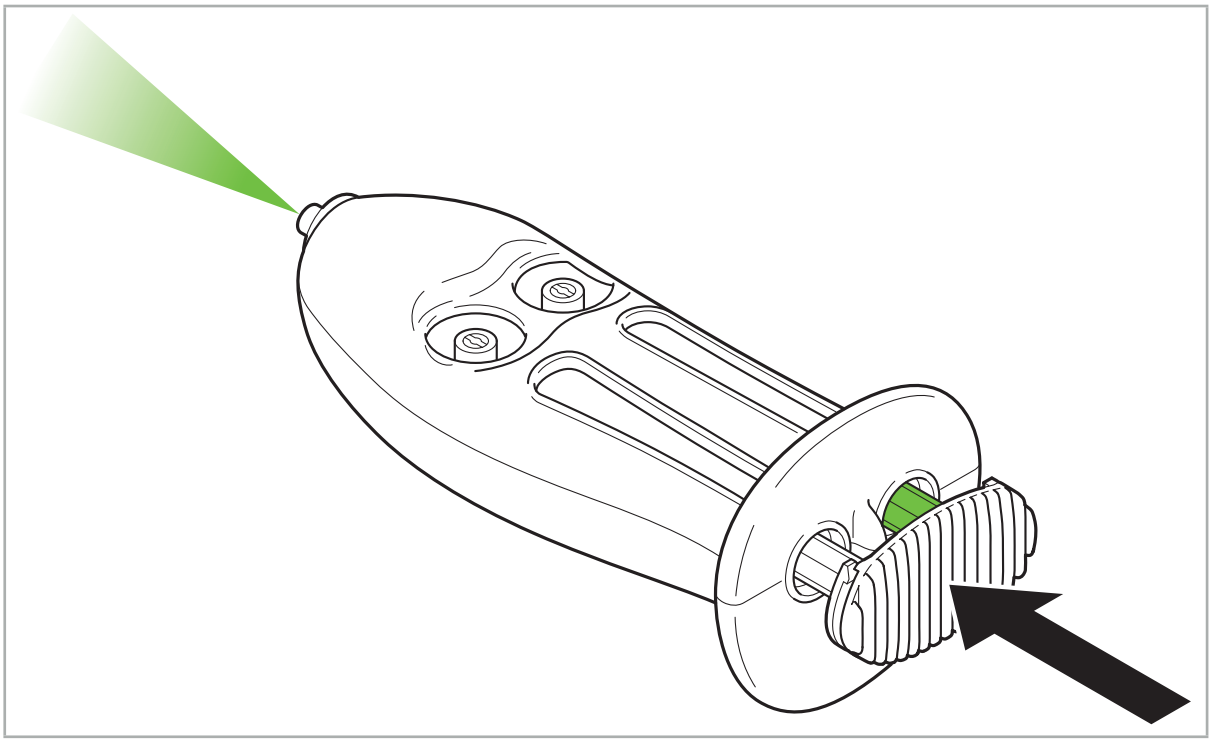
1. For optimal tissue adhesion, ensure that:
    - There are 2 mm to 3 mm of dural margins around the defect.
    - The application site is free of blood, hemostats, or other loose tissue.
    - CSF outflow is minimized.
2. For the applicator with extended tip: To improve treatment site access or visualization, bend the extended applicator tip as needed.
    - Do not bend the extended tip beyond a right angle (90°).
    - After bending, ensure that the sealant is still flowing.
3. Ensure the applicator is on.

4. Hold the applicator with the nozzle pointing upwards.
5. Hold a piece of gauze approximately 5 cm to 10 cm above the nozzle.
6. Apply firm, even pressure to the center of the syringe plunger until the sealant begins to spray out of the nozzle.



Graphic 8: Sealant beginning to spray out

7. Stop squeezing the syringe plunger when a green sealant begins to form on the piece of gauze.
8. Aim the nozzle approximately 2 cm to 4 cm from the treatment site.
9. Apply firm, even pressure to the center of the syringe plunger and dispense the sealant.



Graphic 9: Dispensing the sealant

10. If necessary, interrupt the application by releasing the pressure on the syringe plunger.
    - To avoid clogging: Do not turn off the pump if the application is interrupted.
    - Only turn off the pump at the end of the application.

    If necessary, remove excess sealant from the nozzle by gently wiping with a piece of gauze.

11. Apply the sealant until the layer is approximately 1 mm to 2 mm thick.
    - Refer to *Section 4.2.3 "Gauging the sealant's thickness."*

4.2.3 Gauging the sealant's thickness

Sutured dural closure

Complete coverage of the suture knot will ensure that the minimum application thickness is achieved.

- 4-0, 3-0 and 2-0 sutures are commonly used for dural closure.
- 4-0 is the smallest size with a diameter of 0.15 mm to 0.2 mm.
- A 4-0 suture knot has at least 4 suture widths or a thickness of approximately 0.6 mm to 0.8 mm.

Onlay duraplasty closure

Apply the sealant to cover the duraplasty material and 3 mm to 4 mm of the surrounding native dura. Use the thickness of the duraplasty material as a depth reference.

4.2.4 Finishing the application

1. When the application is complete: If necessary, remove excess sealant beyond the edges of the dural margin with a Penfield probe, with scissors, or by mechanical tearing.
2. Press the on/off button on the underside to switch off the applicator.
3. Dispose of the applicator and the battery properly. Refer to *Section 4.3 "After use."*

4.3 After use

After surgery, the applicator may contain biological substances that pose a threat or are a hazard to the health of living organisms.

 The applicator consists of a plastic housing and electrical components.

Step-by-step instructions of disposal:

▶ Always follow current local recommendations and/or regulations governing environmental protection and risks associated with recycling or disposing of the equipment at the end of its useful life.

ⓘ Only open the battery compartment cover outside the sterile field.

1. To remove the batteries, open the battery compartment cover on the bottom of the applicator.
   - The battery compartment cover is glued shut. If necessary, use a flat instrument to pry open the battery compartment cover.
2. Carefully remove the batteries using appropriate precautions.
   - Contact your local representative for disposal information.
3. Dispose of the applicator in a hospital-approved biohazard container.
   - Do not dispose of the applicator as unsorted municipal waste.

5 Processing

The Adherus AutoSpray Dural Sealant is provided sterile.

▶ Do not process the product.

6 Troubleshooting

Troubleshooting

Problem	Possible cause and solution
There is no sound from the applicator air pump.	The unit is not active, i.e., it is switched off. ▶ Press the on/off button.
The nozzle is blocked or clogged.	The vial adapter hubs were removed before the air pump was turned on. ▶ Wipe the nozzle after use.

7 Technical specifications

7.1 Technical specifications

The following table provides the technical specifications for the product.

Environmental specifications

Condition	Temperature limitation	Relative humidity limitation	Atmospheric pressure limitation
Operation	+5 °C (+41 °F) to +35 °C (+95 °F)	30 % to 75 %	70 kPa to 106 kPa
Storage and transportation	+0 °C (+32 °F) to +30 °C (+86 °F)	9 % to 76 %	50 kPa to 106 kPa

7.2 Electrical specifications

Electrical specifications

Power supply	⎓ Internally powered by 2 × AAA (1.5 V) batteries
Enclosure protection	IPX0 ordinary equipment
Mode of operation	Continuous

7.3 Electromagnetic emissions

The Adherus AutoSpray Dural Sealant applicator is intended for use in the electromagnetic environment specified below.

Electromagnetic emissions

Emissions Test	Compliance	Electromagnetic Environment Guidance
RF emissions CISPR 11	Group 1	Adherus AutoSpray Dural Sealant uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	Adherus AutoSpray Dural Sealant 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	Not applicable	
Voltage fluctuations / flicker emissions IEC 61000-3-3	Not applicable	

7.4 Electromagnetic environment

The Adherus AutoSpray Dural Sealant applicator is intended for use in the electromagnetic environment specified below.

Electromagnetic environment specifications

Testing conducted	Test levels	Compliance levels	Electromagnetic environment – guidance
ESD **IEC 61000-4-2**	Contact ±6 kV Air ±2 kV, ±4 kV, ±8 kV, ±15 kV	Not applicable. Battery-operated system with no digital circuitry.	Floors should be made of wood, concrete, or ceramic tile. For plastic floors, humidity should be at least 30 %.
Electrical fast transient/burst **IEC 61000-4-4**	±2 kV 100 kHz repetition frequency	Not applicable. Battery-operated system.	Mains power quality should be that of a typical commercial or hospital environment.
Surge **IEC 61000-4-5**	±0.5 kV, ±1 kV line-to-line	Not applicable. Battery-operated system.	Mains power quality should be that of a typical commercial or hospital environment.
	±0.5 kV, ±1 kV, ±2 kV line-to-ground		
Power frequency (50/60 Hz) **Magnetic field** **IEC 61000-4-8**	3 A/M 50/60 Hz	Not applicable. Battery-operated system with no magnetically sensitive components.	Mains frequency magnetic fields should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines **IEC 61000-4-11**	< 5 % U_T (> 95 % dip in U_T) for 0,5 cycle	Not applicable. Battery-operated system.	Mains power quality should be that of a typical commercial or hospital environment. Continuous operation is ensured by battery power.
	40 % U_T (60 % dip in U_T) for 5 cycles		
	70 % U_T (30 % dip in U_T) for 25 cycles		
	< 5 % UT (> 95 % dip in U_T) for 5 sec		

ⓘ U_T is the AC mains voltage before the test level is applied.

7.5 Electromagnetic immunity

The Adherus AutoSpray Dural Sealant applicator is intended for use with the electromagnetic immunity specified below.

Immunity Test	IEC 60601 test level	Compliance level	Electromagnetic environment – guidance
Conducted RF IEC 61000-4-6	3 Vrms 6 Vrms (in ISM bands) 150 kHz to 80 MHz	Not applicable. Battery-operated system.	Portable and mobile RF communications equipment should be used no closer to any part of the Adherus AutoSpray Dural Sealant, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. Recommended separation distance $d = 1.2\sqrt{P}$ $d = 2.3\sqrt{P}$ where P is the maximum transmitter output power in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m).
Radiated RF IEC 61000-4-3	80 MHz to 2.7 GHz	3 V/m 80 MHz to 2.7 GHz 80 % AM at 1 kHz	Field strengths from fixed RF transmitters as determined by an electromagnetic site survey[8], should be less than the compliance level in each frequency range[9]. Interference may occur near equipment marked with the following symbol:

ⓘ At 80 MHz and 800 MHz, the higher frequency range applies.

ⓘ These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from buildings, objects, and people.

8 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 Adherus AutoSpray Dural Sealant is used exceeds the applicable RF compliance level above, the Adherus AutoSpray Dural Sealant should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the Adherus AutoSpray Dural Sealant.

9 Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.

7.6 Recommended separation distances between portable and mobile RF communications and Adherus AutoSpray Dural Sealant

Adherus AutoSpray Dural Sealant is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or user of the Adherus AutoSpray Dural Sealant device can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the Adherus AutoSpray Dural Sealant devices as recommended below, according to the maximum output power of the communications equipment.

Rated maximum output power of transmitter	Separation distance according to frequency of transmitter m		
	150 kHz to 80 MHz	80 MHz to 800 MHz	800 MHz to 2.5 GHz
W	$d = 1.2\sqrt{P}$	$d = 1.2\sqrt{P}$	$d = 2.3\sqrt{P}$
0.01	0.12	0.12	0.23
0.1	0.38	0.38	0.73
1	1.2	1.2	2.3
10	3.8	3.8	7.3
100	12	12	23

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.

At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.

These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

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