ReSure® Sealant
Instructions for Use

REF RS 1004-US-5, RS 1004-US-10, RS 1004-US-20

STERILE R
Sterilized using irradiation

Do not re-use

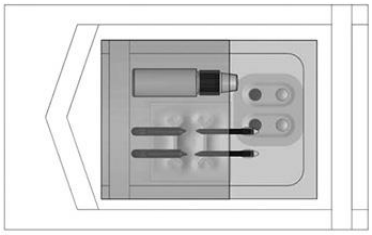
25°C
Upper limit of Temperature

Caution: Federal Law restricts this device to sale by or on the order of a licensed health care practitioner.

Indication: ReSure Sealant is indicated for intraoperative management of clear corneal incisions (up to 3.5mm) with a demonstrated wound leak for which a temporary dry surface can be achieved, in order to prevent postoperative fluid egress from such incisions following cataract surgery with intraocular lens (IOL) placement in adults.

Overview: ReSure Sealant is an in situ formed hydrogel that creates a temporary, soft and lubricious sealant to prevent fluid egress following cataract or intraocular lens placement surgery. ReSure hydrogel typically persists for approximately 1 to 3 days (up to 7 days in some cases), or until re-epithelialization occurs. The cross-linked hydrogel is approximately 89% water at application. ReSure hydrogel softens over time, detaches, and is sloughed off in the tears. ReSure Sealant consists of one plastic dropper bottle filled with diluent solution, a tray with two mixing wells containing lyophilized deposits of reactants (one blue deposit and one white deposit), and two Applicators.

Figure 1



ReSure Sealant is formed by mixing the Diluent with the dried deposits of reactants. The blue color serves as a visualization aid to ensure proper placement of ReSure Sealant, and diffuses from the hydrogel within hours of application.

Warnings:

- Should not be used on actively leaking incisions in which a temporary dry ocular surface cannot be achieved.
- Do not use ReSure Sealant in patients who are allergic to FD&C Blue #1.

Precautions:

- ReSure Sealant is provided sterile. Do not use if packaging or seal has been damaged or opened. Do not re-sterilize.
- The mixing tray, diluent dropper and Applicators should only be used in conjunction with one another.
- The mixing tray, diluent dropper and Applicators are intended for single-use only. Discard opened and unused product.
- Prior to application of ReSure Sealant, ensure incision site is not actively leaking. Remove any standing moisture from the surrounding ocular surface and incision and ensure that the site is dry.
- Use within 30 minutes of removing the mixing tray from foil pouch.
- Prophylactic use of ReSure Sealant on corneal incisions without intraoperative leakage was not evaluated in the clinical study.
- ReSure Sealant will not replace the need for sutures in certain circumstances, including the need for long term mechanical support to the incision.

Clinical Trial Summary

A prospective randomized parallel arm controlled multi-center subject-masked study was conducted to establish non-inferiority of ReSure Sealant to suture(s) to prevent incision leakage from clear corneal incisions. The subject population consisted of patients undergoing uncomplicated unilateral clear corneal cataract surgery with phacoemulsification and implantation of a posterior chamber intraocular lens. Four hundred eighty-eight (305 ReSure Sealant and 183 suture) eyes were enrolled. Subjects were randomized to receive either ReSure Sealant or suture after clear corneal incision leakage was demonstrated post IOL implantation by positive Seidel test. Leakage could be demonstrated either as unprovoked spontaneous leakage, or provoked by a Calibrated Force Gauge (CFG).

NOTE: In the clinical study, ReSure Sealant was compared to use of a single suture closure. Use of additional sutures may have been more optimal to prevent postoperative incision leakage in certain cases.

The event rate for clear corneal incision leakage within the first 7 days after surgery was 4.1% for subjects treated with ReSure Sealant compared to 34.1% for subjects treated with suture. These results established both non-inferiority and superiority of ReSure Sealant compared to suture for the mitigation of cataract incision leaks.

NOTE: The clinical study evaluated use of the device only for single-plane clear corneal incisions up to 3.5mm (reported range of incision width 1.9 mm – 3.5 mm). The potential benefit of ReSure Sealant may not be generalizable to other types of clear corneal incision architecture.

Postoperatively all subjects underwent evaluations at approximately 1 hour and 1, 3, 7, 14, 21 and 28 days post procedure. Additionally, subjects were required to complete the Ocular Comfort Index (OCI) once daily for postoperative days 1-7 and weekly at the Day 14, Day 21, and Day 28 visits. The overall incidence of adverse ocular events reported for subjects treated with ReSure Sealant was lower than for subjects treated with suture (22.7% vs. 45.4%).

ReSure Sealant was reported as "present" on the corneal incision at the post-operative visits as follows:

- 76.1% of eyes at Day 1 post-op
- 31.3% of eyes at Day 3 post-op
- 2.6% of eyes at Day 7 post-op
- 0% of eyes at Day 14 post-op

Thus ReSure Sealant had sloughed off from ~25% of treated eyes prior to the post-op Day 1 visit, and ~70% of treated eyes prior to the post-op Day 3 visit.

In the clinical study, 40% of subjects required use of >1 package of ReSure Sealant to achieve adequate incision coverage. The packaging for ReSure Sealant contains sufficient material for up to 2 applications of the device, if deemed necessary by the surgeon in order to achieve adequate coverage of the incision. However, multiple applications were required for the majority of ReSure treated subjects (Table 1 below).

Table 1: ReSure Sealant Applications Required in the Clinical Study

#Applications	n(%) N=305
0	1 (0.3)
1	54 (17.7)
2	128 (42.0)
3	76 (24.9)
4	32 (10.5)
5	11 (3.6)
6	0 (0.0)
7	2 (0.7)
8	1 (0.3)

Adverse events occurred that are related to ReSure Sealant include corneal astigmatism in the acute post-operative period (1.0%), worsening in best corrected visual acuity by greater than two lines (0.3%), eye pain (0.3%), and foreign body in eye (0.3%). Excluding the ocular AEs in the suture group that were device-related or with "unable to determine" relationship (i.e., subconjunctival hemorrhage, eye irritation, eye pain and others), there was no clinically meaningful difference between the ReSure group (22.7%) and Suture group (21.9%) for the remaining events.

There were two device-related AEs related to ReSure Sealant sloughing off from the incision:

- 1 foreign body in the eye, where 95% of ReSure Sealant sloughed from the incision and needed to be removed with forceps.
- 1 case of eye pain, with ReSure Sealant lifted off of the corneal surface on one side; this event resolved after 4 days.

A summary of the most commonly reported ocular AEs in the clinical study is provided in Table 2 below.

Table 2: Most Commonly Reported Ocular Adverse Events

Adverse Ocular Event	ReSure Sealant (N = 304) n (%)	Suture (N = 183) n (%)
Anterior chamber cells greater than level 1 + persisting beyond Day 7 visit	4 (1.3)	2 (1.1)
Corneal abrasion	1 (0.3)	1 (0.5)
Corneal edema greater than level 1 persisting beyond Day 7 visit	1 (0.3)	2 (1.1)
IOP greater than or equal to 30mmHg or 10mmHg over baseline	16 (5.3)	15 (8.2)
Induced corneal astigmatism with a threshold of 3 diopters	9 (3.0)	3 (1.6)
Posterior vitreous detachment	5 (1.6)	1 (0.5)
Subconjunctival hemorrhage	1 (0.3)	40 (21.9)
Worsening in BCVA greater than 2 lines (greater than 10 letters)	21 (6.9)	9 (4.9)
Cystoid macular edema	0 (0.0)	2 (1.1)
Eye irritation	0 (0.0)	8 (4.4)
Eye pain	8 (2.6)	7 (3.8)
Foreign body sensation	2 (0.7)	7 (3.8)
Suture related complication	0 (0.0)	2 (1.1)

Of the 72 study eyes with post-treatment incision leak within 7 days of surgery, 69 eyes had leak onset during the intra-operative assessment performed after application of ReSure Sealant (11 eyes) or suture placement (58 eyes). There were only 3 subjects with onset of incision leak during the post-op period from Day 1 to Day 7. One ReSure Sealant treated eye leaked at post-op Day 3 with sealant absent, continued to leak at Day 5 and was sutured. Two sutured eyes had incision leak at Day 7 with IOP normal in both (12 and 17 mmHg), no further action was taken.

Refer to the Summary of Safety and Effectiveness Data for complete details about the clinical study.

http://www.accessdata.fda.gov/cdrh_docs/pdf13/P130004b.pdf

Post Approval Study, Device Exposure Registry

The retrospective study utilized data from the American Academy of Ophthalmology's (AAO) Intelligent Research in Sight (IRIS) Registry with analyses conducted by a commercial analytic partner for the IRIS Registry.

Study Objective

Primary objective: to compare the incidence of endophthalmitis within 30 days of any cataract surgery between sites with and without access to ReSure Sealant.

Study Design

Two large cohorts: one cohort consisting of practices with access to ReSure Sealant and a second cohort consisting of practices without access to ReSure Sealant. All cataract surgeries performed in these two cohorts between January 01, 2016 and December 01, 2019 were identified and the patient eyes were followed for 30 days (+ 14-day window) to identify the incidence of endophthalmitis.

Study Population

The study population consisted of subjects with the presence of CPT code(s) in the IRIS database pertaining to an extracapsular cataract removal with insertion of intraocular lens prosthesis. Subjects needed to have at least one visit in the IRIS database within 30 days (+ 14 day window) of the cataract procedure. Practices where the procedure occurred must have contributed data to the IRIS registry for at least 30 days following the date of the procedure. Subjects were > 22 years of age on the date of the procedure.

Data Source

American Academy of Ophthalmology's (AAO) Intelligent Research in Sight (IRIS) Registry.

Total Number of Enrolled Study Sites and Subjects

883 practices were considered to have access to ReSure Sealant while 1,598 practices were not. Per subject eye, 3,534,793 (53%) eyes had cataract procedures at practices with access to ReSure Sealant, while

3,190,205 eyes (47%) had procedures at practices without access.

Summary of the Post Approval Study Results

Between January 01, 2016 and December 01, 2019, 4,259 endophthalmitis cases with specified laterality were identified within 30 days after the cataract surgery. The overall incidence rate of endophthalmitis was 0.633 per 1,000 surgeries. No clinically meaningful difference (i.e., doubling) in incidence rate of endophthalmitis was found between eyes treated at practices with access to ReSure Sealant compared with practices without access to ReSure Sealant. The results are summarized in Table 3.

Table 3: Incidence of Endophthalmitis Rate by Practice Access to ReSure

Practices with Access to ReSure	Practices without Access to ReSure
Endophthalmitis Incidence per 1,000 Surgeries (95% CI)	
0.609 (0.583, 0.635)	0.660 (0.632, 0.688)

While the observed rate of endophthalmitis for practices with access to ReSure Sealant was lower than the observed rate for practices without access to ReSure Sealant, this difference was not clinically meaningful.

In addition, no clinically meaningful difference (i.e., doubling) in incidence of endophthalmitis was found between eyes treated at practices with access to ReSure Sealant, compared with practices without access to ReSure Sealant, among eyes that had routine cataract surgeries or among eyes that had complex cataract surgeries. These results are summarized in Table 4.

Table 4: Incidence of Endophthalmitis Rate by Cataract Surgery Type

	Practices with Access to ReSure	Practices without Access to ReSure
Endophthalmitis Incidence per 1,000 Surgeries (95% CI)		
Routine Cataract Procedure	0.572 (0.546, 0.598)	0.614 (0.586, 0.642)
Complex Cataract Procedure	1.082 (0.955, 1.209)	1.219 (1.08, 1.357)

Study Strength and Weaknesses

This large research study quantified the incidence of endophthalmitis after cataract surgery in a cohort of over 6.7 million cataract procedures. We found the overall incidence of endophthalmitis within 30 days after cataract surgery to be 0.633 per 1,000 cataract surgeries (95% CI: 0.614 - 0.652).

The primary limitation of the research method was the use of the ecologic study design. With this study design, the use of ReSure Sealant in the cohort with access to ReSure Sealant was assumed and cannot be verified for a given cataract surgery as use is not routinely coded in EHR medication tables. Since the objective of the research was to identify whether or not use of ReSure Sealant causes an increase risk in endophthalmitis, this design can only be used to identify if the cohort with access to ReSure Sealant has any clinically significant increased risk of endophthalmitis; it cannot predict the impact of access to ReSure Sealant at a patient level. The second limitation is that each cohort was matched at the physician level not the practice level. It was assumed if a physician was matched to a practice, then all practices to which that physician belonged were deemed to have access to ReSure Sealant. Patients may not have access to ReSure Sealant if the physician did not use ReSure Sealant at all associated practices, or if the physician did not use ReSure Sealant in all cataract procedures that were performed at the practice. Thus, results cannot show a direct, causal link between endophthalmitis rate and ReSure Sealant use.

Detailed Preparation

CAUTION: Prior to application of ReSure Sealant, ensure incision site is not actively leaking. Remove any standing moisture from the surrounding conjunctival surface and ensure that the site is dry.

A. Preparing the Tray with Addition of Diluent

1. Using sterile technique, transfer the contents of the Tyvek pouch onto the sterile field.
2. Tear open the foil pouches and carefully remove the Mixing Tray and Diluent Dropper.
3. Remove end cap from the Diluent Dropper and keep cap.
4. Select one channeled well for mixing and add two drops of the Diluent to the blue deposit. Do not add any drops to the white deposit in the same channeled well (Fig. 2).

B. Mixing and Applying ReSure Sealant

NOTE: Mixing and applying ReSure Sealant must be complete in less than 30 seconds.

1. Use the Applicator to thoroughly and rapidly mix the solutions using a back and forth motion (about 5 seconds; Fig. 3).
2. Holding the Applicator handle with the side edge of the foam tip facing down, gently dip the foam tip into the solution, picking up the material (Fig. 4).
3. Apply ReSure Sealant over the entire length, width and edges of the incision, ensuring full coverage of the margins (Fig. 5).

Fig. 2

Fig. 3

Fig. 4

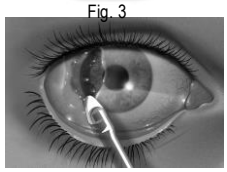


Fig. 5

NOTE: Stop manipulation of the Applicator if liquid material stranding is observed. If application to the incision site was not completed prior to stranding, prepare the second channeled well and reapply.

NOTE: The device packaging contains material for 2 applications. In the clinical trial, 40% of subjects required >2 applications (i.e., >1 package). It may be necessary to open additional packages to achieve full coverage.

CAUTION: Each Applicator is intended for single-use only. If a second application is required, use a new Applicator.

CAUTION: When full coverage of the incision cannot be achieved (including incisions with brisk/copious leaks, or incisions for which a temporary dry surface cannot be achieved), and for incisions at higher risk of postoperative wound leak, ReSure Sealant should not be used and suture placement should instead be considered.

4. Delay introduction of any ophthalmic drops to the ocular surface for approximately 30 seconds after application of ReSure Sealant to ensure polymerization of the material and complete adherence and coverage of the target area.

NOTE: ReSure Sealant may be removed carefully with forceps if necessary.

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Patent #8, 961, 501 B2