Outcomes in cataract surgery using ReSure® Sealant for the intraoperative management of clear corneal incisions:

Results from a registry evaluation of ReSure Sealant for pre-specified ocular adverse events

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BACKGROUND

ReSure Sealant is a polyethylene glycol (PEG) hydrogel that creates a temporary surface barrier to seal clear corneal incisions following cataract or IOL placement surgery

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

In clinical practice, there is broad diversity in surgical technique and perioperative care with respect to cataract extraction

Within this current post-approval registry study, the safety of ReSure Sealant, used under commercial use conditions was evaluated to provide broader experience with the device

STUDY OBJECTIVES

To collect post-approval data relative to the incidence of pre-specified Ocular Adverse Events for cataract surgery patients treated with ReSure Sealant, specifically anterior chamber inflammation, hypotony, ocular discomfort, and/or surgical re-intervention

METHODS

Patient Population

Entry criteria for enrollment into the registry are presented in Table 1

Table 1: Study Population

Inclusion Criteria	Exclusion Criteria
≥ 22 years of age	Repeat participation in current ReSure Sealant post-approval study
Scheduled clear corneal cataract surgery with phacoemulsification and implantation of a posterior chamber IOL	Participation in another clinical trial during the follow-up period that could confound the treatment or outcomes of this post-approval study
Willing and able to comply with study requirements	Lack of application of ReSure Sealant

Primary Endpoints

Study endpoints are outlined in Table 2

Table 2: Primary Study Endpoints

Proportion of patients experiencing Adverse Ocular Events in the postoperative follow-up period:
• **Anterior chamber cells** (greater than 1+ grade, persisting at Visit 2, ≥ Day 20)
• **Hypotony** (≤ 5 mmHg)
• **Ocular discomfort** (an OCI score greater than 51.7 or a within-person increase from baseline of greater than 37.8)
• **Surgical reintervention**

Study Design

- Prospective, multicenter, single-arm observational post-approval registry study
- Conducted at 22 sites in the United States
- Patients underwent cataract surgery using the surgeon's standard techniques; if ReSure Sealant was applied, patients were enrolled in the study
- ReSure Sealant was prepared and applied in accordance with the product's accompanying Instructions for Use
- Patients were sequentially enrolled in this study, and were evaluated:
  - **Visit 1:** Day 1 to Day 3
  - **Visit 2:** Day 20 to Day 40
- Assessments at each visit:
  - Evaluation of Adverse Ocular Events, Primary Endpoint
  - Intraocular Pressure (IOP)
  - Slit lamp examination (SLE) with fluorescein staining (including an assessment of ReSure Sealant presence) (Table 3)
  - Ocular Comfort Index (OCI) questionnaire

Table 3: Grading Scale for SLE Observations

Corneal Staining/Erosion	Stromal Edema	Epithelial Edema	Anterior Chamber Cells* (Grade and Number of Cells in Field**)
0 None; No staining	**0** None; Transparent and clear or less than mild	**0** None; Normal/no microcysts)	**0** <1 Cell
1 Mild; Slight or punctate fluorescein staining confined to a small focus	**1** Mild; Dull glassy appearance	**1** Trace; 1-20 microcysts	**0.5+** 1-5 Cells
2 Moderate; Regionally dense fluorescein staining with underlying structure moderately visible	**2** Moderate; Dull glassy appearance of epithelium with large number of vacuoles	**2** Mild; 21 to 50 microcysts	**1+** 6-15 Cells
3 Severe; Marked fluorescein staining or epithelial loss	**3** Severe; Epithelial bullae and/or stromal edema, localized or diffuse, with or without stromal striae	**3** Moderate; 50 to 100 microcysts	**2+** 16-25 Cells
		4 Severe; >100 microcysts	**3+** 26-50 Cells
			4+ >50 Cells

* SUN Working Group grading scheme; ** Field size is a 1 mm by 1 mm slit beam

- Additional data collected included:
  - Number of ReSure Sealant devices used
  - Number of ReSure Sealant applications
  - ReSure Sealant lot numbers
  - Concomitant suture use (before and/or after use of ReSure Sealant)
  - Additional procedure(s) performed

Statistical Analysis

- All analyses of the primary endpoints and of safety were based on all subjects who received at least one application of ReSure Sealant on the study eye
- Achievement of the primary endpoint was based on statistical analysis of the true proportion of eyes exhibiting any adverse ocular event occurring less than or equal to 7.5%

RESULTS

Patient Disposition

- 626 sequential subjects were enrolled in the post-approval registry
  - 64 screen failures: 15 due to preoperative screening exclusion, 3 due to intraoperative exclusion (surgeon did not apply ReSure Sealant), and 46 due to other reasons
  - 7 subjects did not complete the study
  - No subjects were discontinued due to an adverse event
- Enrolled subjects ranged in age from 31 to 92 years (mean 68.2 years)
- There was a slightly greater proportion of women (57.8%)
- The patient population was mostly White (90.7%) with predominantly brown or blue eyes (45% and 31.9% respectively)

Primary Endpoint Analysis

Table 4: Results, Primary Endpoints

Adverse Ocular Event	ReSure Sealant (n=619)	*P* Value
Anterior chamber cells, n (%)	5 (0.8%)	<0.0001
Hypotony, n	0	<0.0001
Ocular discomfort, n (%)	4 (0.6%)	<0.0001
Surgical reintervention, n(%)	3 (0.5%)	<0.0001

- Primary efficacy endpoint results are presented in Table 4
- A total of 12 endpoint adverse ocular events were reported for 12 subjects within the cohort of 626 subjects (1.9%)
- Eleven of the 12 events were determined to be related to cataract surgery (one exception was for a subject who received an incorrectly-powered lens implant, which was deemed neither device nor surgery related)
- Severity of the Adverse Ocular Events reported is listed in Table 5; most events were mild or moderate in severity, and no event was considered severe
- The true proportion of all primary adverse ocular events was less than 7.5%
- There were no serious adverse events or events deemed related to use of ReSure Sealant
- Table 5 shows the incidence of Adverse Ocular Events for this post-approval study, as compared to the incidence reported in the pivotal trial

Other Assessments

Intraocular Pressure

- There was a slight increase in mean IOP at Visit 1 (3.2 mmHg); however, by postoperative Visit 2, there was a mean decrease from Baseline (-0.5 mmHg)
- Twenty-six subjects (4.2%) experienced a postoperative spike in IOP of > 30 mmHg at Visit 1, but in all cases the IOP normalized to baseline by Visit 2

Other Assessments (con't)

Slit Lamp Examination

- SLE observations were consistent with previous studies
- ReSure Sealant was not found to promote corneal or anterior chamber inflammation and was well tolerated by ocular tissues

Table 5: Severity of Adverse Ocular Events

Adverse Ocular Event	Severity			
	Mild	Moderate	Severe	TOTAL
Anterior chamber cells, n (%)	5 (100.0%)	0	0	5 (100%)
Hypotony, n	0	0	0	0
Ocular discomfort, n (%)	1 (25.0%)	3 (75.0%)	0	4 (100%)
Surgical reintervention, n(%)	1 (33.3%)	2 (66.7%)	0	3 (100%)

Table 5: Adverse Ocular Events, Post-Approval and Pivotal Trials

Adverse Ocular Event	ReSure Sealant PA (n=619)	ReSure Sealant PT (n=304)
Anterior chamber cells, n (%)	5 (0.8%)	4 (1.3%)
Hypotony, n	0	0
Ocular discomfort*, n (%)	4 (0.6%)	8 (1.2%)
Surgical reintervention, n(%)	3 (0.5%)	1 (0.3%)

* Termed "Eye Pain" for ReSure Sealant PT

CONCLUSIONS

Collectively, the assessments performed throughout the follow-up period did not raise any safety concerns and provided continued evidence that ReSure Sealant is well tolerated by the human eye. No safety issues were identified. The frequency of primary endpoint Adverse Ocular Events was well below the pre-specified threshold of 7.5%. Results of this post-approval registry study confirm that the ReSure Sealant can be used safely by ophthalmologists

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