Juveena®

SPACE AND TIME TO HEAL

JUVEENA® HYDROGEL SYSTEM
INSTRUCTIONS FOR USE



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SECTION 1

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician or licensed practitioner.

Indication:

The Juveena® Hydrogel System is indicated for use in adult women to reduce the incidence and severity of intrauterine adhesion formation following hysteroscopic adhesiolysis for symptomatic moderate to severe intrauterine adhesions.

The Rejoni Acorn Catheter is indicated to access the uterine cavity and deliver the Juveena® Hydrogel solution into the uterine cavity.

Contraindications:

The Juveena® Hydrogel System should not be used in presence of:

- Hemorrhage
- Active pelvic infection
- Sexually transmitted disease
- Pregnancy
- Known hypersensitivity or allergy to Polyethylene Glycol (PEG) or FD&C Blue #1 dye

Warnings:

- This procedure should only be performed by a physician or properly licensed practitioner trained in gynecologic diagnostic and interventional techniques.
- Use only with the delivery system provided with the Juveena® kit, Rejoni Acorn Catheter.
- Do not use if the PEG powder is not free flowing (i.e. appears solidified).
- Administer the hydrogel within 1 hour of preparation.
- The Juveena® Hydrogel System is provided sterile. Do not use if packaging or seal has been damaged or opened. Do not re-sterilize.
- The Juveena® Hydrogel System is intended for single patient use only. Discard opened and unused product.
- Patients should be informed to avoid pregnancy during the first complete menstrual cycle subsequent to the treatment with the Juveena® Hydrogel System
- Potential adverse reactions include discomfort, pain/cramping, infection, local inflammatory reaction, and allergic reaction.

Precautions:

- The safety and effectiveness of Juveena® has not been established following hysteroscopic procedures other than adhesiolysis of moderate to severe adhesions.

- The safety and effectiveness of the Juveena® Hydrogel System has not been established in patients undergoing thermal endometrial ablation.
- Proper adjustment of catheter length is necessary for optimal device performance. If the catheter extends to or presses against the uterine fundus, catheter clogging may occur.
- The gel will form within seconds. Pausing instillation will result in clogging of the Y-Connector and catheter.

Product Overview:

The Juveena® Hydrogel System consists of components for preparation of a synthetic, temporary hydrogel intrauterine spacer and related system components packaged for single use only. The separately pouched Rejoni Acorn Catheter is to be used to instill the Juveena® hydrogel to fill the uterine cavity and separate traumatized surfaces following adhesiolysis of symptomatic moderate to severe intrauterine adhesions.

The intrauterine spacer is formed *in-situ* by mixing two solutions, the Precursor and the Accelerator. The Precursor solution is formed through the mixing of the Diluent solution (Trilysine buffer solution) with the PEG powder. The Accelerator solution is a salt buffer solution. When mixed, the solutions cross-link to form a temporary, conforming intrauterine spacer.

The Juveena® Hydrogel System is used after hysteroscopic adhesiolysis of symptomatic moderate to severe intrauterine adhesions as a temporary intrauterine spacer to separate traumatized uterine surfaces and to reduce intrauterine adhesion formation. Within approximately 14 - 21 days following application the hydrogel undergoes hydrolysis and is discharged through the cervix and vagina.

The Juveena® Hydrogel System is provided sterile and consists of the following components:

Powder Vial, with blue label		Vial Adapter	
Diluent Syringe, with blue label		Accelerator Syringe	
Y-Connector		Syringe Holder	
Plunger Cap			

The Rejoni Acorn Catheter is used to access the uterine cavity for the delivery of Juveena® hydrogel solution.

Rejoni Acorn Catheter	

SECTION 2

Juveena® Hydrogel Pivotal Clinical Study

The Juveena® Hydrogel System Pivotal Study was a multicenter, randomized, subject- and evaluator-blinded clinical study designed to evaluate the safety and effectiveness of the Juveena® Hydrogel System in reducing the incidence and severity of intrauterine adhesions (IUAs) following adhesiogenic transcervical gynecological procedures (TCGPs), specifically adhesiolysis of moderate to severe IUAs or myomectomy resulting in trauma to the endometrial basalis due to the positioning and/or size of the fibroid(s) within the endometrial cavity. Within this study 150 subjects were randomized using a 2:1 ratio: 99 to the Juveena® HS group where the TCGP was performed followed by instillation of the Juveena® Hydrogel and 51 to the Control group (TCGP alone). Approximately 8 weeks after the TCGP, subjects underwent a second look hysteroscopy (SLH) to allow for evaluation for the presence and severity of IUAs. Randomization was stratified by surgery type (adhesiolysis or myomectomy). A total of 102 subjects underwent adhesiolysis (67 Juveena® and 35 control) and 48 subjects underwent myomectomy (32 Juveena® and 16 control).

Fifteen (15) centers across the United States participated, including both hospital-based and clinic-based sites. All investigators were board-certified in Obstetrics & Gynecology and experienced in hysteroscopic surgery.

Inclusion Criteria (Pre-operative)

1. Premenopausal female subjects ≥ 18 years of age
2. Candidate for one of the following hysteroscopic procedures:
    a. Adhesiolysis: Subjects with demonstrated IUA who typically presented with one or a combination of infertility, recurrent pregnancy loss, and light or absent periods. To qualify, there was a confirmed hysteroscopic diagnosis of moderate to severe intrauterine adhesions using the March IUA classification scale.
    b. Myomectomy: Symptomatic subjects who required hysteroscopic myomectomy of one or more FIGO Type 1 or Type 2 fibroid(s) ≥1 cm in diameter, measured in 2 planes, and, in the opinion of the Investigator, the resulting intrauterine tissue trauma associated with the myomectomy would be adhesiogenic due to the positioning and/or size of the fibroid(s) within the endometrial cavity. Examples of adhesiogenic conditions occurred when fibroids were located in the fundal, ostial, or lower segment areas where the fibroid was in contact or near contact with opposing uterine walls OR when opposing wall fibroids were in contact or near contact with each other.
3. Subject agreed to all protocol requirements including returning for specified visits within intervals identified within the protocol.
4. Subject was willing to undergo an SLH at the Week 8 visit and was thought to gain benefit from the SLH (i.e., reducing adhesion related complications).
5. Subject agreed to abstain from sexual intercourse or use a reliable form of barrier contraception following the study procedure through the Week 8 visit.
6. The subject was willing to comply with the Investigator's post-operative instructions including the post-operative medication regimen.

7. Subject had signed the IRB/EC approved informed consent.

Exclusion Criteria (Pre-operative)

Subjects who met any of the following criteria were not eligible for participation in the study:

1. Postmenopausal
2. IUD present at time of TCGP (unless removed before or during the study TCGP).
3. Past history of endometrial cancer OR atypical endometrial hyperplasia (endometrial intraepithelial neoplasia).
4. Planned intrauterine intervention post-TCGP through the Week 8 visit.
5. Recent intrauterine surgery within 6 weeks of the planned study procedure.
6. Pregnant (positive pregnancy test) or lactating
7. Pregnancy was within the last 6 weeks prior to the planned study procedure for a first trimester loss (≤13 weeks gestation) or within 3 months of the planned study procedure for all other pregnancies.
8. Active sexually transmitted infection (e.g., positive testing for gonorrhea/chlamydia), or genital or urinary tract infection at screening (e.g., cervicitis, vaginitis, endometritis, salpingitis, or cystitis) or other active and/or systemic infection.
9. Use of systemic corticosteroids within 1 week of the study procedure
10. Treated with a long-acting injectable hormone/hormone implant that would still have been active at the time of the TCGP.
11. Known allergy to FD&C No.1 dye or PEG
12. Known clotting defects or bleeding disorders
13. Any other general health or mental condition that in the opinion of the investigator could represent an increased risk for the subject, affect the primary outcomes of this study and/or impact the subject's ability to comply with protocol requirements.
14. Participated or was considering participation in a clinical trial of another investigational drug or device during this study.

Exclusionary Criteria (Intraoperative)

1. Incidental finding of preoperative exclusionary criteria or determination that the subject did not meet preoperative inclusion criteria.
2. Inability to access the uterine cavity during attempted hysteroscopy.
3. Concomitant myomectomy and adhesiolysis of moderate or severe adhesions during the study procedure.
4. TCGP-related adverse event that in the opinion of the investigator would make continuation in the study not in the best interest of the subject.
5. Incomplete TCGP:
    - For Adhesiolysis: Inability to confirm a normalized endometrial cavity that includes visualization of the ostial areas.
    - For Myomectomy: inability to remove the targeted myoma(s) leaving no residual tumor.

Study Objectives/Hypotheses

Primary Effectiveness Endpoint:

The primary effectiveness endpoint of this study was the percentage of subjects with no IUA based on an independent Central Review Committee (CRC) of 3 experienced surgical gynecologists via assessment of paired video-recordings of the baseline TCGP and Week 8 SLH. For myomectomy subjects, "No IUA" was defined as the complete absence of adhesions at the SLH (i.e., no de novo adhesions following the procedure). For adhesiolysis subjects, "No IUA" required that there be no new or recurrent IUAs at SLH when compared with the end-of-procedure video. The hypothesis was one of superiority, i.e., there would be a greater percentage of subjects with no IUA at the Week 8 SLH in the group treated with the hydrogel compared to the Control. This endpoint was to be evaluated using a one-sided significance level of 0.025.

Secondary Effectiveness Endpoints

The study had the following pre-specified secondary endpoints and associated hypotheses. Secondary endpoints were analyzed hierarchically, contingent on the success of the primary hypothesis. Using this approach each endpoint was evaluated using a one-sided 0.025 alpha level.

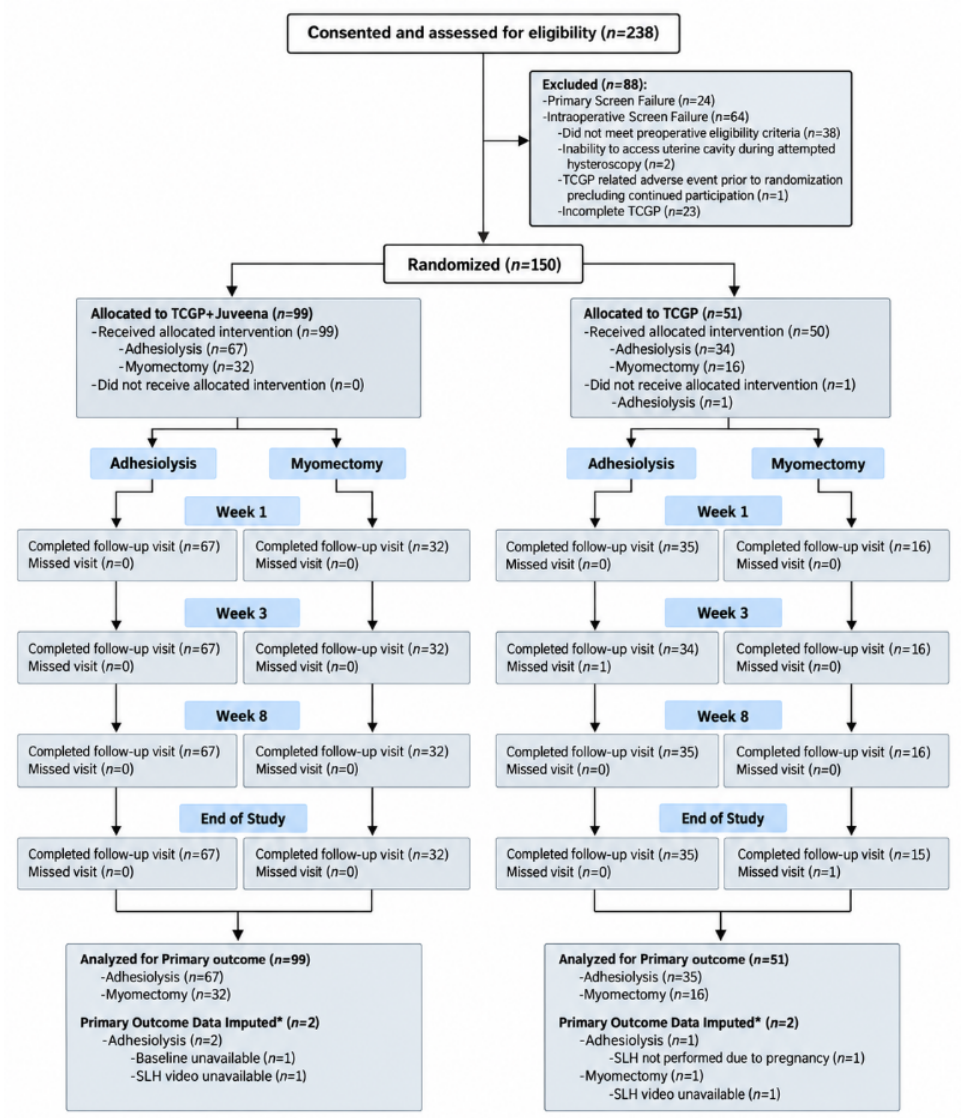
1. Change in IUA Severity Category from Baseline to SLH in Adhesiolysis Subjects: Categorical analysis of change in IUA severity from baseline to SLH was determined from comparing the investigator-assessed IUA severity at baseline (at the time of the TCGP) with the Week 8 SLH severity assessed by the independent blinded CRC from the video recording. IUA Severity was scored using the March IUA classification system (reference **Table 1**). The hypothesis evaluated was that IUA severity would differ between the treatment groups in the subpopulation undergoing adhesiolysis:

Table 1. March IUA Severity Scoring
Severity Scoring
Minimal: < ¼ of uterine cavity involved; thin or filmy adhesions; ostial areas and upper fundus minimally involved or clear.
Moderate: ¼ to ¾ of the uterine cavity involved; no agglutination of walls -adhesions only; ostial areas and upper fundus only partially occluded.
Severe: > ¾ of uterine cavity involved; agglutination of walls or thick bands; ostial areas and upper cavity occluded

2. IUA Severity: Categorical analysis of severity of adhesions at the SLH for all subjects (adhesiolysis and myomectomy combined): the proportion of subjects categorized in each IUA severity category (none, minimal, moderate, severe) at the SLH as determined by the independent CRC. The hypothesis evaluated is that distribution of IUA severity will differ amongst treatment groups.
3. Primary Effectiveness Endpoint at a 5% Superiority Margin: The analysis of the primary effectiveness endpoint was repeated at a superiority margin of 5%.

Figure 1 provides patient accounting of all subjects in the study including screen failures. Pre-specified primary and secondary effectiveness analyses were based on the intent-to-treat (ITT) population, with missing data imputed for four subjects without paired baseline and SLH videos. Other data presentations for the adhesiolysis population were based on the full analysis set (FAS) population, which includes all subjects analyzed as randomized with SLH data available.

Figure 1: Patient Accounting



Patient Demographics

The study population's demographic characteristics are summarized in Table 2.

Table 2.Demographics				
	Adhesiolysis and myomectomy – ITT Population		Adhesiolysis only – FAS Population	
	TCGP + Juveena® N=99	TCGP N=51	TCGP + Juveena® N=67	TCGP N=35
Age (years)				
Mean ± SD (N)	36.8 ± 4.87 (99)	37.0 ± 6.01 (51)	35.8 ± 3.88 (67)	35.6 ± 5.40 (35)
Median (Min, Max)	36.0 (26.0, 51.0)	37.0 (24.0, 49.0)	36.0 (28.0, 46.0)	35.0 (24.0, 45.0)
Ethnicity				
Hispanic/Latino	9.1% (9/99)	12.0% (6/50)	10.4% (7/67)	17.6% (6/34)
Not Hispanic/Latino	90.9% (90/99)	88.0% (44/50)	89.6% (60/67)	82.4% (28/34)
Race [1]				
American Indian or Alaska Native	1.0% (1/99)	0.0% (0/51)	0.0% (0/67)	0.0% (0/35)
Asian	8.1% (8/99)	7.8% (4/51)	4.5% (3/67)	8.6% (3/35)
Black or African American	21.2% (21/99)	21.6% (11/51)	14.9% (10/67)	11.4% (4/35)
Native Hawaiian/Pacific Islander	0.0% (0/99)	2.0% (1/51)	0.0% (0/67)	0.0% (0/35)
White	65.7% (65/99)	62.7% (32/51)	77.6% (52/67)	71.4% (25/35)
Other	6.1% (6/99)	2.0% (1/51)	4.5% (3/67)	2.9% (1/35)
Unknown/Not Reported	0.0% (0/99)	5.9% (3/51)	0.0% (0/67)	5.7% (2/35)
BMI (kg/m^2)				
Mean ± SD (N)	27.7 ± 6.83 (99)	27.9 ± 5.66 (51)	26.8 ± 7.07 (67)	27.6 ± 5.61 (35)
Median (Min, Max)	25.6 (17.9, 49.5)	27.8 (18.6, 41.3)	24.8 (17.9, 49.5)	27.0 (19.1, 39.6)
Total Number of Pregnancies				
Mean ± SD (N)	1.9 ± 1.84 (99)	1.8 ± 1.85 (51)	1.8 ± 1.38 (67)	1.8 ± 1.33 (35)
Median (Min, Max)	1.0 (0.0, 10.0)	1.0 (0.0, 9.0)	1.0 (0.0, 6.0)	1.0 (0.0, 5.0)
Number of Abortions & Miscarriages (<20 weeks gestation)				
Mean ± SD (N)	1.2 ± 1.23 (82)	1.4 ± 1.39 (40)	1.2 ± 1.26 (60)	1.3 ± 1.35 (31)
Median (Min, Max)	1.0 (0.0, 5.0)	1.0 (0.0, 5.0)	1.0 (0.0, 5.0)	1.0 (0.0, 5.0)
Prior Intrauterine Procedure [2]				
No Prior Intrauterine Procedure	20.2% (20/99)	23.5% (12/51)	1.5% (1/67)	8.6% (3/35)
Any Prior Intrauterine Procedure	79.8% (79/99)	76.5% (39/51)	98.5% (66/67)	91.4% (32/35)
Adhesiolysis	45.6% (36/79)	51.3% (20/39)	54.5% (36/66)	62.5% (20/32)
Myomectomy	17.7% (14/79)	12.8% (5/39)	10.6% (7/66)	3.1% (1/32)
Polypectomy	8.9% (7/79)	5.1% (2/39)	9.1% (6/66)	3.1% (1/32)
Septoplasty	2.5% (2/79)	5.1% (2/39)	3.0% (2/66)	6.3% (2/32)
Lesion/Cyst Excision	1.3% (1/79)	2.6% (1/39)	0.0% (0/66)	3.1% (1/32)
Biopsy	6.3% (5/79)	5.1% (2/39)	7.6% (5/66)	6.3% (2/32)
Endometriosis Excision	0.0% (0/79)	0.0% (0/39)	0.0% (0/66)	0.0% (0/32)
Prior Pregnancy-related D&C	55.7% (44/79)	64.1% (25/39)	59.1% (39/66)	71.9% (23/32)
Other Prior Intrauterine Procedure	10.1% (8/79)	23.1% (9/39)	10.6% (7/66)	25.0% (8/32)
Baseline Menses Status				
Subject experiencing menses?	89.9% (89/99)	86.3% (44/51)	85.1% (57/67)	82.9% (29/35)
Subject not experiencing menses?	10.1% (10/99)	13.7% (7/51)	14.9% (10/67)	17.1% (6/35)
For those experiencing menses, is subject experiencing dysmenorrhea?				
Yes	36.0% (32/89)	38.6% (17/44)	28.1% (16/57)	33.3% (9/27)
No	61.8% (55/89)	56.8% (25/44)	70.2% (40/57)	66.7% (18/27)
Not Reported	2.2% (2/89)	4.5% (2/44)	1.7% (1/57)	0.0% (0/27)
Menses Cycle Pattern				
Regular	23.2% (23/99)	29.4% (15/51)	31.3% (21/67)	28.6% (10/35)
Amenorrhea	10.1% (10/99)	13.7% (7/51)	14.9% (10/67)	17.1% (6/35)
Hypomenorrhea	33.3% (33/99)	27.5% (14/51)	44.8% (30/67)	40.0% (14/35)
Hypermenorrhea	26.3% (26/99)	21.6% (11/51)	3.0% (2/67)	5.7% (2/35)
Not Classifiable	7.1% (7/99)	7.8% (4/51)	6.0% (4/67)	8.6% (3/35)
Fertility Status [3]				
Subject Desires to Bear Children	84.5% (82/97)	88.2% (45/51)	100.0% (67/67)	94.3% (33/35)
Subject Infertile	67.1% (55/82)	62.2% (28/45)	68.7% (46/67)	69.7% (23/33)

[1] Subjects can report more than one race so numbers may be greater than the total.
[2] Number and percentage of patients who have at least 1 of the given types of prior pelvic surgery. Denominator is based on the number of patients who had a prior pelvic surgery/intervention.
[3] The denominator for “Subject Desires to Bear Children” includes subjects with an evaluable response to this baseline assessment. The denominator for “Subject Infertile” includes only subjects who reported a desire to bear children.
SD: standard deviation

Surgical Characteristics

Surgical indications and characteristics are summarized in Table 3. In the ITT population 99 subjects were assigned to receive treatment with Juveena® Hydrogel (67 adhesiolysis and 32 myomectomy) and 51 subjects were assigned to the Control treatment arm (35 adhesiolysis and 16 myomectomy). One subject randomized to Control received treatment with Juveena® (in accordance with the ITT methodology, the Control subject who received Juveena® was analyzed within the Control group as randomized).

Table 3. Surgical Characteristics

	Adhesiolysis and myomectomy – ITT Population		**Adhesiolysis only – FAS Population**	
	TCGP + Juveena® N=99	**TCGP N=51**	**TCGP + Juveena® N=67**	**TCGP N=35**
Indication				
Adhesiolysis	67.7% (67/99)	68.6% (35/51)	100.0% (67/67)	100.0% (35/35)
Myomectomy	32.3% (32/99)	31.4% (16/51)	0.0% (0/67)	0.0% (0/35)
Indication: Adhesiolysis				
Baseline Adhesion Severity (Investigator assessment)				
Moderate			56.7% (38/67)	65.7% (23/35)
Severe			43.3% (29/67)	34.3% (12/35)
Instruments used during Adhesiolysis [1]				
Blunt or sharp dissection			94.0% (63/67)	100.0% (35/35)
Electrocautery (Cut and/or Coag)			3.0% (2/67)	2.9% (1/35)
Morcellation			13.4% (9/67)	11.4% (4/35)
Multiple instruments [3]			10.4% (7/67)	14.3% (5/35)
Adhesions remaining at End of Surgery			0.0% (0/67)	0.0% (0/35)
Indication: Myomectomy				
Kissing Fibroids	9.4% (3/32)	18.8% (3/16)		
Number of Myoma Resected				
Mean ± SD (N)	1.6 ± 1.29 (32)	1.4 ± 0.73 (16)		
Median (Min, Max)	1.0 (1.0, 7.0)	1.0 (1.0, 3.0)		
Breakdown of Location [2]				
Anterior	15.7% (8/51)	8.7% (2/23)		
Posterior	7.8% (4/51)	13.0% (3/23)		
Fundal	17.6% (9/51)	26.1% (6/23)		
Lower Segment	25.5% (13/51)	26.1% (6/23)		
Left Lateral	5.9% (3/51)	13.0% (3/23)		
Right Lateral	11.8% (6/51)	13.0% (3/23)		
Left Ostial Region	3.9% (2/51)	0.0% (0/23)		
Right Ostial Region	11.8% (6/51)	0.0% (0/23)		
Minimum Diameter of Myoma (mm) [2]				
Mean ± SD (N)	18.3 ± 11.72 (51)	19.3 ± 9.06 (23)		
Median (Min, Max)	20.0 (3.0, 54.0)	17.5 (5.0, 37.0)		
Maximum Diameter of Myoma (mm) [2]				
Mean ± SD (N)	22.3 ± 13.43 (51)	23.5 ± 12.86 (23)		
Median (Min, Max)	20.0 (5.0, 60.0)	20.0 (5.0, 50.0)		
FIGO Class				
FIGO Class I [2]	21.6% (11/51)	26.1% (6/23)		
FIGO Class II [2]	78.4% (40/51)	73.9% (17/23)		
Instruments used during Myomectomy [1]				
Sharp dissection	9.4% (3/32)	6.3% (1/16)		
Electrocautery (Cut and/or Coag)	81.3% (26/32)	81.3% (13/16)		
Morcellation	12.5% (4/32)	12.5% (2/16)		
Other	0.0% (0/32)	6.3% (1/16)		

Table 3. Surgical Characteristics				
	Adhesiolysis and myomectomy – ITT Population		Adhesiolysis only – FAS Population	
	TCGP + Juveena® N=99	TCGP N=51	TCGP + Juveena® N=67	TCGP N=35
Multiple instruments [3]	3.1% (1/32)	6.3% (1/16)		
Concomitant Laparoscopic Procedure Performed	2.0% (2/99)	0.0% (0/51)	1.5% (1/67)	0.0% (0/35)
Concomitant Polypectomy	8.1% (8/99)	2.0% (1/51)	4.5% (3/67)	0.0% (0/35)

[1] More than 1 instrument could be used and therefore, it may add up to more than the total N patients treated.
[2] N is the number of myoma across all patients within the treatment group.
[3] Multiple instruments option is not mutually exclusive from the instruments listed above.
SD: standard deviation

Hydrogel Instillation Procedural Characteristics (Table 4)

For those subjects assigned to receive Juveena® hydrogel, the mean uterine cavity length measured was 7.6 cm (±1.37), with a median of 7.0 cm and a range of 5.0 to 12.0 cm. The mean hydrogel volume instilled was 9.5 mL (±1.32), with a median of 10.0 mL; most subjects received the maximum volume of 10 mL. Based on Investigators' determination, ultrasound assessment confirmed complete filling of the uterine cavity in 94.8% of cases, with only one subject (1.0%) showing incomplete filling, and 4 cases (4.1%) reported as unable to be determined. For these 4 cases, the volume of gel instilled relative to the uterine cavity dimensions suggested that the cavity was completely filled.

Instillation was rapid, with a mean duration of 0.9 minutes (median 0.5 minutes; range 0.1–7.0 minutes). Investigators rated the procedure as "neutral" to "very easy" in nearly all cases (92.0%), with a mean ease-of-use score of 4.1 on a 5-point scale.

Table 4. Hydrogel Administration Procedural Characteristics - TCGP + Juveena®		
	Adhesiolysis and myomectomy – ITT Population	**Adhesiolysis only – FAS Population**
	TCGP + Juveena® N=99	**TCGP + Juveena® N=67**
Uterine Cavity Length Measurement (cm)		
Mean ± SD (N)	7.6 ± 1.37 (99)	7.1 ± 1.04 (67)
Median (Min, Max)	7.0 (5.0, 12.0)	7.0 (5.0, 10.0)
Volume of Hydrogel Instilled in Uterus (mL)		
Mean ± SD (N)	9.5 ± 1.32 (99)	9.3 ± 1.55 (67)
Median (Min, Max)	10.0 (3.0, 10.0)	10.0 (3.0, 10.0)
Received Full Volume of Hydrogel (10mL)	82.8% (82/99)	76.1% (51/67)
Based on Ultrasound, Did Hydrogel Appear to Completely Fill the Uterine Cavity?		
Yes	94.8% (92/97)	93.8% (61/65)
No	1.0% (1/97)	0.0% (0/65)
Unable to determine (UTD)	4.1% (4/97)	6.2% (4/65)
Instillation Procedure Time (minutes)		
Mean ± SD (N)	0.9 ± 1.02 (97)	1.1 ± 1.16 (65)
Median (Min, Max)	0.5 (0.1, 7.0)	0.8 (0.1, 7.0)
Ease of Instillation		
1 - Very Difficult	1.0% (1/99)	1.5% (1/67)
2 - Difficult	7.1% (7/99)	10.4% (7/67)
3 - Neutral	17.2% (17/99)	20.9% (14/67)
4 - Easy	29.3% (29/99)	37.3% (25/67)
5 - Very Easy	45.5% (45/99)	29.9% (20/67)
Mean ± SD (N)	4.1 ± 1.00 (99)	3.8 ± 1.02 (67)
SD: standard deviation		

Safety Results

There were no unanticipated adverse device events. In the Safety Population, 115 treatment-emergent adverse events (TEAEs) were reported in 59/100 (59.0%) Juveena® subjects and 51 TEAEs were reported in 21/50 (42.0%) Control subjects. Most events were designated as mild or moderate, with severe events uncommon.

Table 5 presents all TEAEs by primary attribution. Among Juveena®-treated subjects, 53 TEAEs in 38 subjects (38.0%) were assessed as possibly related to the study device, 8 TEAEs in 7 subjects (7.0%) as probably related, and 1 TEAE in 1 subject (1.0%) as definitely related. Under the prespecified primary-attribution convention, TEAEs assessed as probably or definitely related to the study device were assigned a primary attribution of Study Device.

Table 5. Treatment Emergent Adverse Events by Primary Attribution [1][2] Safety Population				
	TCGP + Juveena® N = 100		**TCGP N = 50**	
Primary Attribution / MedDRA SOC / Preferred Term	**Number of Events N**	**% Participants with Event % (n/N)**	**Number of Events N**	**% Participants with Event % (n/N)**
Total Study Device TEAEs	**9**	**8.0% (8/100)**	**0**	**0.0% (0/50)**
Product issues	1	1.0% (1/100)	0	0.0% (0/50)
Device expulsion	1	1.0% (1/100)	0	0.0% (0/50)
Reproductive system and breast disorders	8	7.0% (7/100)	0	0.0% (0/50)

Table 5. Treatment Emergent Adverse Events by Primary Attribution [1][2] Safety Population				
	TCGP + Juveena® N = 100		TCGP N = 50	
Primary Attribution / MedDRA SOC / Preferred Term	Number of Events N	% Participants with Event % (n/N)	Number of Events N	% Participants with Event % (n/N)
Dysmenorrhea	1	1.0% (1/100)	0	0.0% (0/50)
Pelvic discomfort	2	2.0% (2/100)	0	0.0% (0/50)
Pelvic pain	2	2.0% (2/100)	0	0.0% (0/50)
Uterine spasm	3	3.0% (3/100)	0	0.0% (0/50)
Total TCGP Procedure TEAEs	**65**	**43.0% (43/100)**	**22**	**32.0% (16/50)**
Gastrointestinal disorders	17	13.0% (13/100)	3	4.0% (2/50)
Abdominal discomfort	1	1.0% (1/100)	1	2.0% (1/50)
Abdominal distension	3	2.0% (2/100)	0	0.0% (0/50)
Abdominal pain	11	10.0% (10/100)	2	4.0% (2/50)
Diarrhea	1	1.0% (1/100)	0	0.0% (0/50)
Hemorrhoids	1	1.0% (1/100)	0	0.0% (0/50)
Gastrointestinal signs and symptoms	1	1.0% (1/100)	0	0.0% (0/50)
Abdominal discomfort	1	1.0% (1/100)	0	0.0% (0/50)
Injury, poisoning and procedural complications	7	6.0% (6/100)	6	10.0% (5/50)
Procedural nausea	3	2.0% (2/100)	1	2.0% (1/50)
Procedural pain	4	4.0% (4/100)	5	10.0% (5/50)
Metabolism and nutrition disorders	1	1.0% (1/100)	0	0.0% (0/50)
Decreased appetite	1	1.0% (1/100)	0	0.0% (0/50)
Musculoskeletal and connective tissue disorders	0	0.0% (0/100)	1	2.0% (1/50)
Back pain	0	0.0% (0/100)	1	2.0% (1/50)
Nervous system disorders	1	1.0% (1/100)	1	2.0% (1/50)
Dizziness	1	1.0% (1/100)	1	2.0% (1/50)
Renal and urinary disorders	1	1.0% (1/100)	0	0.0% (0/50)
Dysuria	1	1.0% (1/100)	0	0.0% (0/50)
Reproductive system and breast disorders	35	28.0% (28/100)	10	18.0% (9/50)
Dysmenorrhea	2	2.0% (2/100)	0	0.0% (0/50)
Heavy menstrual bleeding	2	2.0% (2/100)	0	0.0% (0/50)
Ovarian vein thrombosis	1	1.0% (1/100)	0	0.0% (0/50)
Pelvic discomfort	7	6.0% (6/100)	1	2.0% (1/50)
Pelvic pain	1	1.0% (1/100)	5	8.0% (4/50)
Uterine hemorrhage	1	1.0% (1/100)	1	2.0% (1/50)
Uterine pain	1	1.0% (1/100)	0	0.0% (0/50)
Uterine spasm	13	12.0% (12/100)	3	6.0% (3/50)
Vaginal hemorrhage	6	6.0% (6/100)	0	0.0% (0/50)
Vulvovaginal pruritus	1	1.0% (1/100)	0	0.0% (0/50)
Respiratory, thoracic and mediastinal disorders	1	1.0% (1/100)	0	0.0% (0/50)
Pulmonary edema	1	1.0% (1/100)	0	0.0% (0/50)
Skin and subcutaneous tissue disorders	1	1.0% (1/100)	1	2.0% (1/50)
Pruritus	0	0.0% (0/100)	1	2.0% (1/50)
Urticaria	1	1.0% (1/100)	0	0.0% (0/50)
Total Other Concomitant Therapy TEAEs	**7**	**6.0% (6/100)**	**5**	**8.0% (4/50)**
Blood and lymphatic system disorders	0	0.0% (0/100)	1	2.0% (1/50)
Anemia	0	0.0% (0/100)	1	2.0% (1/50)
Gastrointestinal disorders	1	1.0% (1/100)	0	0.0% (0/50)

Table 5. Treatment Emergent Adverse Events by Primary Attribution [1][2] Safety Population				
	TCGP + Juveena® N = 100		TCGP N = 50	
Primary Attribution / MedDRA SOC / Preferred Term	Number of Events N	% Participants with Event % (n/N)	Number of Events N	% Participants with Event % (n/N)
Abdominal distension	1	1.0% (1/100)	0	0.0% (0/50)
Injury, poisoning and procedural complications	0	0.0% (0/100)	1	2.0% (1/50)
Procedural nausea	0	0.0% (0/100)	1	2.0% (1/50)
Investigations	1	1.0% (1/100)	0	0.0% (0/50)
Oxygen saturation decreased	1	1.0% (1/100)	0	0.0% (0/50)
Nervous system disorders	1	1.0% (1/100)	0	0.0% (0/50)
Migraine	1	1.0% (1/100)	0	0.0% (0/50)
Psychiatric disorders	0	0.0% (0/100)	1	2.0% (1/50)
Emotional disorder	0	0.0% (0/100)	1	2.0% (1/50)
Reproductive system and breast disorders	4	4.0% (4/100)	1	2.0% (1/50)
Uterine spasm	1	1.0% (1/100)	0	0.0% (0/50)
Vaginal discharge	1	1.0% (1/100)	0	0.0% (0/50)
Vaginal hemorrhage	2	2.0% (2/100)	0	0.0% (0/50)
Vulvovaginal pain	0	0.0% (0/100)	1	2.0% (1/50)
Vascular disorders	0	0.0% (0/100)	1	2.0% (1/50)
Hot flush	0	0.0% (0/100)	1	2.0% (1/50)
Total Comorbidities TEAEs	**9**	**6.0% (6/100)**	**12**	**16.0% (8/50)**
Blood and lymphatic system disorders	0	0.0% (0/100)	1	2.0% (1/50)
Iron deficiency anemia	0	0.0% (0/100)	1	2.0% (1/50)
Gastrointestinal disorders	3	2.0% (2/100)	1	2.0% (1/50)
Abdominal pain	1	1.0% (1/100)	0	0.0% (0/50)
Constipation	1	1.0% (1/100)	0	0.0% (0/50)
Diarrhea	0	0.0% (0/100)	1	2.0% (1/50)
Hemorrhoidal hemorrhage	1	1.0% (1/100)	0	0.0% (0/50)
General disorders and administration site conditions	0	0.0% (0/100)	1	2.0% (1/50)
Feeling hot	0	0.0% (0/100)	1	2.0% (1/50)
Infections and infestations	0	0.0% (0/100)	3	4.0% (2/50)
Urinary tract infection	0	0.0% (0/100)	3	4.0% (2/50)
Injury, poisoning and procedural complications	1	1.0% (1/100)	0	0.0% (0/50)
Muscle strain	1	1.0% (1/100)	0	0.0% (0/50)
Investigations	1	1.0% (1/100)	1	2.0% (1/50)
Cardiac murmur	0	0.0% (0/100)	1	2.0% (1/50)
Hemoglobin decreased	1	1.0% (1/100)	0	0.0% (0/50)
Nervous system disorders	0	0.0% (0/100)	2	4.0% (2/50)
Headache	0	0.0% (0/100)	2	4.0% (2/50)
Reproductive system and breast disorders	3	3.0% (3/100)	3	4.0% (2/50)
Dysmenorrhea	1	1.0% (1/100)	0	0.0% (0/50)
Heavy menstrual bleeding	0	0.0% (0/100)	1	2.0% (1/50)
Pelvic discomfort	1	1.0% (1/100)	0	0.0% (0/50)
Pelvic pain	1	1.0% (1/100)	1	2.0% (1/50)
Vaginal hemorrhage	0	0.0% (0/100)	1	2.0% (1/50)
Vascular disorders	1	1.0% (1/100)	0	0.0% (0/50)
Hypertension	1	1.0% (1/100)	0	0.0% (0/50)

Table 5. Treatment Emergent Adverse Events by Primary Attribution [1][2] Safety Population				
	TCGP + Juveena® N = 100		TCGP N = 50	
Primary Attribution / MedDRA SOC / Preferred Term	**Number of Events N**	**% Participants with Event % (n/N)**	**Number of Events N**	**% Participants with Event % (n/N)**
Total Other TEAEs	**25**	**21.0% (21/100)**	**12**	**16.0% (8/50)**
Gastrointestinal disorders	4	4.0% (4/100)	2	4.0% (2/50)
Abdominal discomfort	1	1.0% (1/100)	0	0.0% (0/50)
Abdominal pain	2	2.0% (2/100)	0	0.0% (0/50)
Abdominal pain lower	1	1.0% (1/100)	0	0.0% (0/50)
Diarrhea	0	0.0% (0/100)	1	2.0% (1/50)
Nausea	0	0.0% (0/100)	1	2.0% (1/50)
General disorders and administration site conditions	2	1.0% (1/100)	0	0.0% (0/50)
Pain	1	1.0% (1/100)	0	0.0% (0/50)
Pyrexia	1	1.0% (1/100)	0	0.0% (0/50)
Infections and infestations	7	6.0% (6/100)	3	6.0% (3/50)
Bacterial vaginosis	1	1.0% (1/100)	0	0.0% (0/50)
COVID-19	1	1.0% (1/100)	1	2.0% (1/50)
Nasopharyngitis	1	1.0% (1/100)	0	0.0% (0/50)
Pharyngitis streptococcal	1	1.0% (1/100)	0	0.0% (0/50)
Sinusitis	1	1.0% (1/100)	0	0.0% (0/50)
Upper respiratory tract infection	1	1.0% (1/100)	0	0.0% (0/50)
Urinary tract infection	1	1.0% (1/100)	0	0.0% (0/50)
Vulvovaginal mycotic infection	0	0.0% (0/100)	2	4.0% (2/50)
Injury, poisoning and procedural complications	4	3.0% (3/100)	1	2.0% (1/50)
Contusion	1	1.0% (1/100)	0	0.0% (0/50)
Fall	1	1.0% (1/100)	0	0.0% (0/50)
Post procedural hemorrhage	1	1.0% (1/100)	0	0.0% (0/50)
Procedural pain	1	1.0% (1/100)	1	2.0% (1/50)
Musculoskeletal and connective tissue disorders	1	1.0% (1/100)	1	2.0% (1/50)
Arthralgia	1	1.0% (1/100)	0	0.0% (0/50)
Groin pain	0	0.0% (0/100)	1	2.0% (1/50)
Nervous system disorders	1	1.0% (1/100)	1	2.0% (1/50)
Headache	0	0.0% (0/100)	1	2.0% (1/50)
Tension headache	1	1.0% (1/100)	0	0.0% (0/50)
Reproductive system and breast disorders	4	4.0% (4/100)	2	4.0% (2/50)
Pelvic discomfort	1	1.0% (1/100)	0	0.0% (0/50)
Uterine spasm	0	0.0% (0/100)	1	2.0% (1/50)
Vaginal discharge	1	1.0% (1/100)	0	0.0% (0/50)
Vaginal odor	1	1.0% (1/100)	0	0.0% (0/50)
Vulval disorder	0	0.0% (0/100)	1	2.0% (1/50)
Respiratory, thoracic and mediastinal disorders	0	0.0% (0/100)	1	2.0% (1/50)
Sinus congestion	0	0.0% (0/100)	1	2.0% (1/50)
Skin and subcutaneous tissue disorders	3	3.0% (3/100)	1	2.0% (1/50)
Dermatitis	1	1.0% (1/100)	0	0.0% (0/50)
Dermatitis contact	0	0.0% (0/100)	1	2.0% (1/50)
Onychoclasis	1	1.0% (1/100)	0	0.0% (0/50)
Urticaria	1	1.0% (1/100)	0	0.0% (0/50)

Table 5. Treatment Emergent Adverse Events by Primary Attribution [1][2] Safety Population				
	TCGP + Juveena® N = 100		TCGP N = 50	
Primary Attribution / MedDRA SOC / Preferred Term	Number of Events N	% Participants with Event % (n/N)	Number of Events N	% Participants with Event % (n/N)
[1] Events that are adjudicated as either a cascading or non-event are not included.				
[2] The primary attribution is deemed 'study device' if the AE is either definitely or probably related to the study device.				
MedDRA SOC: Medical Dictionary for Regulatory Activities System Organ Class				

TEAEs were most commonly attributed to the TCGP procedure, occurring in 43/100 (43.0%) Juveena® subjects and 16/50 (32.0%) Control subjects. Nine events in 8/100 (8.0%) Juveena® subjects were primarily attributed to the study device. All study-device-attributed events were non-serious; most were mild or moderate and all resolved with no intervention or conservative medical management.

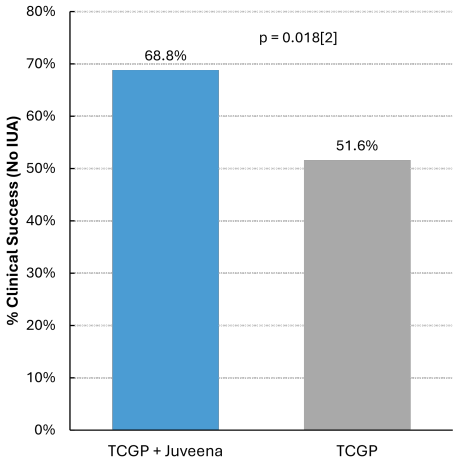
Table 6 summarizes the six serious adverse events (SAEs) reported in five subjects (3 Juveena®, 2 Control), including adjudicated relatedness, timing after the index procedure, and resolution status.

Table 6. Serious Adverse Events – Safety Population						
SAE Event	Treatment Group [1]	Adjudicated Relatedness to Device	Procedure	Adjudicated Relatedness to Procedure	Time After Index Procedure	Resolution Status
Iron deficiency anemia	Control	Not applicable (Control)	Myomectomy	Unrelated	0 days	Resolved
Severe uterine cramping (uterine spasm)	TCGP + Juveena®	Unlikely related	Adhesiolysis	Definitely related	0 days	Resolved
Pulmonary edema	TCGP + Juveena®	Possibly related	Myomectomy	Probably related	0 days	Resolved
Ovarian vein thrombosis	TCGP + Juveena®	Unlikely related	Adhesiolysis	Probably related	5 days	Ongoing at end of study
Severe menstrual/vaginal bleeding	Control	Not applicable (Control)	Myomectomy	Unlikely related	47 days	Resolved
Severe menstrual/vaginal bleeding	Control	Not applicable (Control)	Myomectomy	Unlikely related	62 days	Ongoing at end of study
[1] Treatment group reflects treatment received in the Safety Population. Relatedness, timing, and outcome are based on completed adjudication.						

Effectiveness Results

Primary Endpoint: 68.8% in the Juveena® group were defined as a clinical success (no IUA) compared with 51.6% in the Control group (one-sided p value of 0.018), **demonstrating statistical superiority** of Juveena® relative to Control (see Figure 2).

Figure 2. Juveena® Study Primary Endpoint (percentage of subjects with no IUA) ITT Population - Imputed [1]



[1] The missing data mechanism for "No IUA" status is Missing at Random (MAR) for all missing data and is imputed using fully conditional specification (FCS) logistic regression. Statistics reported are combined across 50 imputed data sets, using standard multiple imputation techniques.

[2] A common risk difference one-sided Z-test stratified by TCGP randomization strata/indication (myomectomy vs. adhesiolysis) was used to test the null hypothesis at a one-sided 0.025 level of significance for each imputation. The overall one-sided p-value is combined across 50 imputed data sets, using standard multiple imputation techniques.

In a subgroup analysis, among subjects in the FAS undergoing adhesiolysis, 61.5% (40/65) of Juveena® subjects were free of intrauterine adhesions at Week 8 compared with 38.2% (13/34) of Control subjects. Among subjects undergoing myomectomy, 84.4% (27/32) of Juveena® subjects were free of intrauterine adhesions at Week 8 compared with 80.0% (12/15) of Control subjects. The study was not designed or powered to establish effectiveness within each surgical indication separately; these subgroup results are descriptive.

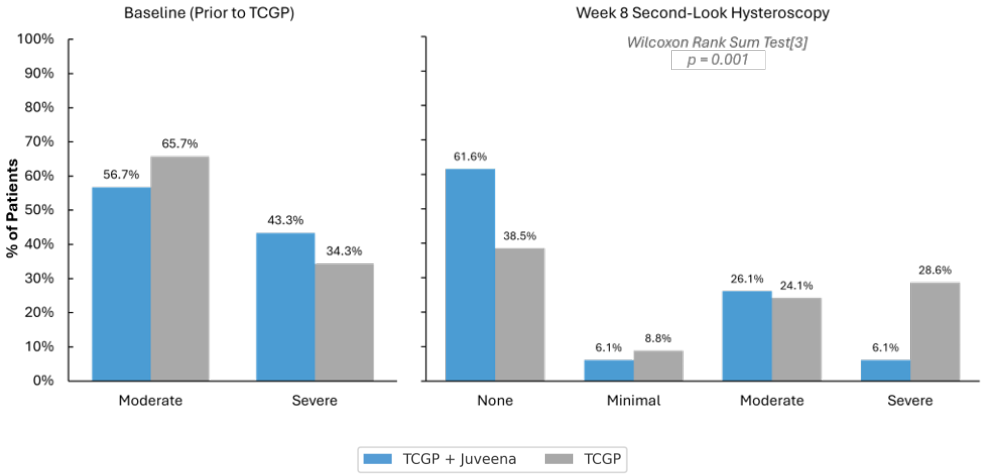
Secondary Endpoints

Pre-specified secondary endpoints were analyzed hierarchically, contingent on the success of the primary hypothesis. The change in IUA severity was tested first, followed by IUA severity, and finally the primary effectiveness endpoint at a 5% superiority margin. If any test in the sequence failed, subsequent endpoints would not have been formally tested.

Secondary Endpoint #1: Change In IUA Severity Among Adhesiolysis Subjects

As shown in Figure 3, in adhesiolysis subjects, Juveena® treatment resulted in a statistically significant reduction in adhesion severity at Week 8 compared with Control ($p = 0.001$), with fewer severe adhesions and more subjects free from IUA.

Figure 3: Change in IUA Severity Category – March Classification [1] ITT Population (Imputed) [2] – Adhesiolysis Patients

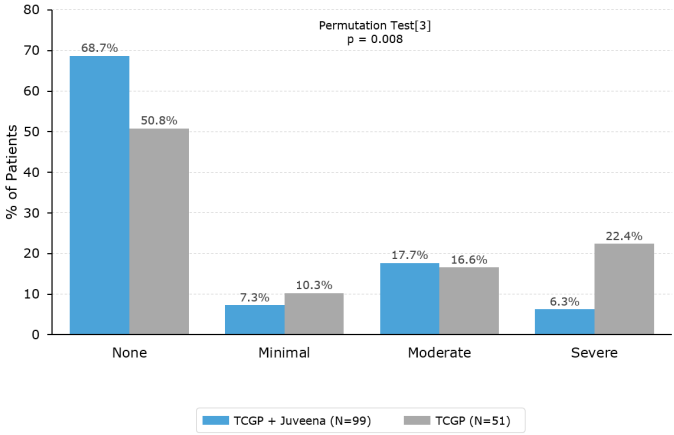


[1] The March et al. Classification is used to assess the severity of adhesions. This classification includes the following levels: severe (> 3/4 of uterine cavity involved; agglutination of walls or thick bands; ostial areas and upper cavity occluded), moderate (1/4 to 3/4 of the uterine cavity involved; no agglutination of walls – adhesions only; ostial areas and upper fundus only partially occluded), and minimal (< 1/4 of uterine cavity involved; thin or filmy adhesions; ostial areas and upper fundus minimally involved or clear).
[2] The missing data mechanism for IUA severity is Missing at Random (MAR) for all missing data and is imputed using fully conditional specification (FCS) ordinal regression. Statistics reported are combined across 50 imputed data sets, using standard multiple imputation techniques.
[3] A Wilcoxon Rank Sum test data was used to test the null hypothesis at a one-sided 0.025 level of significance for each imputation. Each of the 50 p-values will be transformed to standard normal Z statistics using Rubin's combining rules. The standard normal Z test statistics was combined across all imputed datasets using standard multiple imputation theory to obtain an overall p-value for the Wilcoxon Rank Sum test.

Secondary Endpoint #2: IUA Severity Among All Subjects

Analysis of IUA severity across all subjects (adhesiolysis and myomectomy combined) showed that Juveena® was associated with more subjects with no IUA and, when IUA were present, lower severity compared with the Control group (p=0.008); Figure 4.

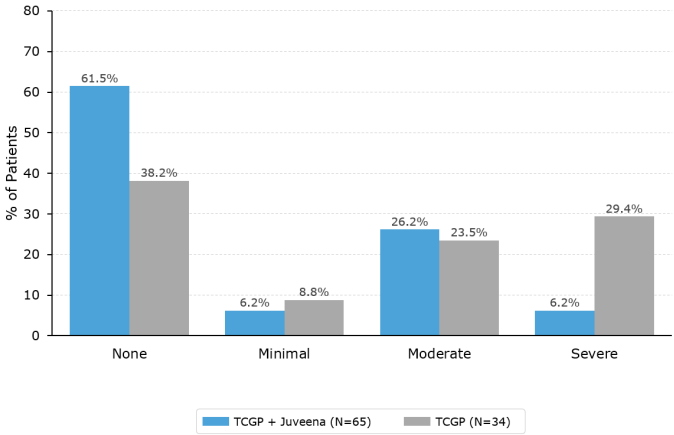
Figure 4: IUA Severity Category at Week 8 SLH- March Classification [1] – ITT Population (Imputed [2])



[1] The March et al. Classification is used to assess the severity of adhesions. This classification includes the following levels: severe (> 3/4 of uterine cavity involved; agglutination of walls or thick bands; ostial areas and upper cavity occluded), moderate (1/4 to 3/4 of the uterine cavity involved; no agglutination of walls – adhesions only; ostial areas and upper fundus only partially occluded), and minimal (< 1/4 of uterine cavity involved; thin or filmy adhesions; ostial areas and upper fundus minimally involved or clear).
[2] The missing data mechanism for IUA severity is Missing at Random (MAR) for all missing data and is imputed using fully conditional specification (FCS) ordinal regression. Statistics reported are combined across 50 imputed data sets, using standard multiple imputation techniques.
[3] A one-way permutation test for the independence of ordinal data will be used to test the null hypothesis at a one-sided 0.025 level of significance for each imputation. Each of the 50 p-values will be transformed to standard normal Z statistics using Rubin's combining rules. The standard normal Z test statistics was combined across all imputed datasets using standard multiple imputation theory to obtain an overall p-value for the one-sided permutation test.

In the FAS adhesiolysis subgroup, 61.5% (40/65) of Juveena® subjects had no IUA at Week 8 compared with 38.2% (13/34) of Control subjects. In addition, the proportion of subjects with severe adhesions was numerically lower in the Juveena® group (6.2% [4/65]) than in the Control group (29.4% [10/34]); the overall distribution of IUA severity is shown in Figure 5.

Figure 5: IUA Severity Category at Week 8 SLH- March Classification [1] – FAS Population, Adhesiolysis Only



[1] The March et al. Classification is used to assess the severity of adhesions. This classification includes the following levels: severe (> 3/4 of uterine cavity involved; agglutination of walls or thick bands; ostial areas and upper cavity occluded), moderate (1/4 to 3/4 of the uterine cavity involved; no agglutination of walls – adhesions only; ostial areas and upper fundus only partially occluded), and minimal (< 1/4 of uterine cavity involved; thin or filmy adhesions; ostial areas and upper fundus minimally involved or clear).

Secondary Endpoint #3: Evaluation of 5% Superiority Margin

In evaluation of the primary endpoint within the framework of a 5% superiority margin, the one-sided p-value did not reach statistical significance at the 0.025 threshold (p=0.071). Therefore, superiority beyond 5% was not statistically confirmed.

SECTION 3

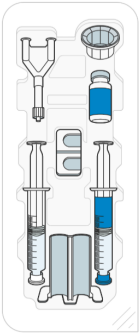
Juveena® Hydrogel System Preparation

The Juveena® Hydrogel System is prepared as follows:

A. Aseptic Examination and Transfer
B. Preparing the Catheter
C. Preparing the Precursor Syringe
D. Assembling the delivery components for instillation
E. Positioning the catheter and instillation

A. Aseptic Examination and Transfer

1. Shake and inspect the Powder Vial through the clear pouch and tray to verify the PEG powder is free flowing. Discard and replace the device if the PEG powder is not free flowing.
2. Inspect the hydrogel pouch sterile barrier for damage. Discard and replace the device if any damage is found.
3. Using sterile technique, open the pouch and transfer the tray of the Juveena® Hydrogel System into the sterile field.
4. Open the Tyvek lid of the tray.
5. Verify all components are present within the tray.

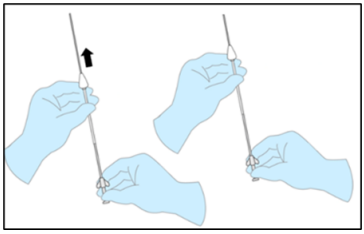


6. Inspect the catheter pouch sterile barrier for damage. Discard and replace the device if any damage is found.
7. Using sterile technique, open the pouch and transfer the catheter into the sterile field.

NOTE: Use sterile technique through the remaining procedural steps.

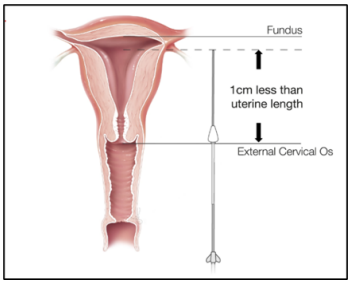
B. Preparing the Catheter

1. Holding the luer in one hand and below the acorn in the other, adjust the catheter.



2. Adjust length to 1 cm less than the measured uterine length from back of acorn to tip of catheter.

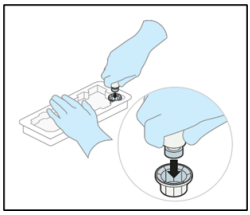
CAUTION: Proper adjustment of catheter length is necessary for optimal device performance. If the catheter extends to or presses against the uterine fundus, catheter clogging may occur.



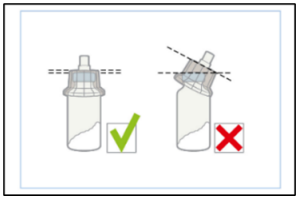
3. Set aside the catheter within the sterile field.

C. Preparing the Precursor Syringe

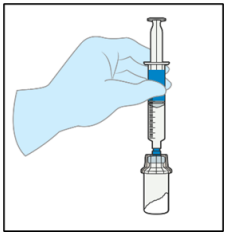
1. Pick up the Powder Vial from the tray.
2. With the Vial Adapter in the tray, and using one hand to stabilize tray, use force to push the Powder Vial straight down to snap the Vial Adapter in place.



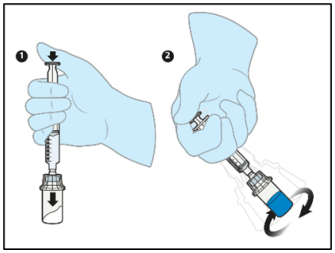
3. After the snap occurs, verify the Vial Adapter is fully seated.



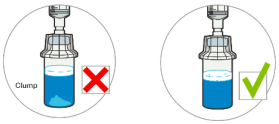
4. Pick up the Diluent Syringe (blue label), remove the blue cap from the Diluent Syringe, and discard.
5. Attach the Diluent Syringe (blue label) to the Powder Vial (blue label). Ensure the luer connection is properly tightened.



6. Inject syringe contents into the vial.



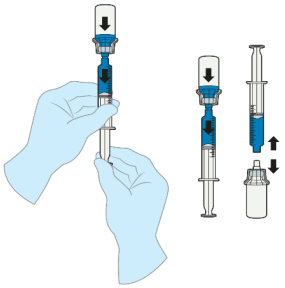
7. Swirl the vial/syringe assembly until the powder is completely dissolved. This may take approximately 1 minute.



8. If solution appears cloudy with bubbles, set aside for bubbles to disperse.

NOTE: Use the device within 60 minutes of mixing. If time exceeds 60 minutes, discard and replace the device.

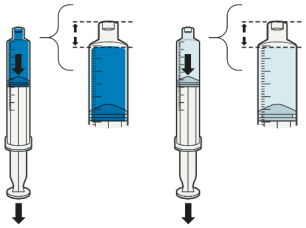
9. Invert the vial/syringe assembly and draw 5 mL of Blue Precursor back into the syringe.



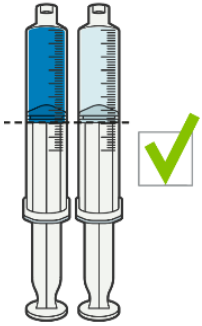
10. Invert and unscrew the Syringe from the Powder Vial and discard the vial. This is the Blue Precursor Syringe.

D. Assembling the Delivery Components for Instillation

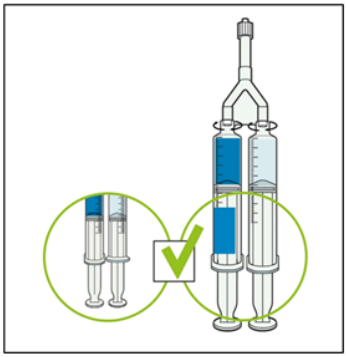
1. Remove the cap from the Accelerator Syringe.
2. Pull back the syringe plunger to break the seal and expel liquid as needed so that 5 mL remains in the syringe.
3. Pull back each syringe to leave a small gap to avoid clogging Y-Connector during set-up.



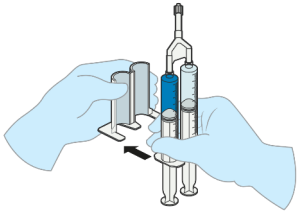
4. Check that the Blue Precursor and the Accelerator Syringe fluid levels are equal.



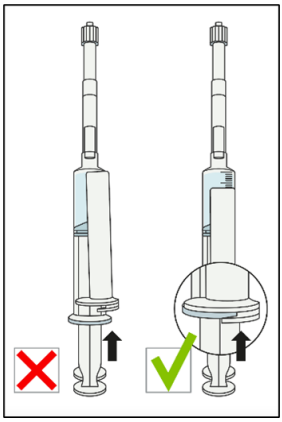
5. With the syringes held upright, attach Precursor and Accelerator Syringes to the Y-Connector. The syringe flanges do not need to be in the same orientation; either aligned with each other or rotated independently is acceptable, as long as the flanges do not contact or overlap. Do not overtighten the syringes onto the Y-Connector.



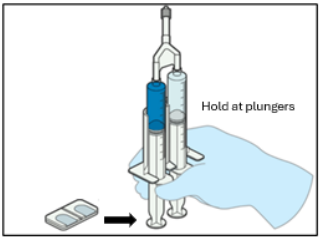
6. With the syringes held upright attach the Syringe Holder to the syringe barrels.



NOTE: Confirm flange alignment to ensure the syringes are properly seated in the Syringe Holder.

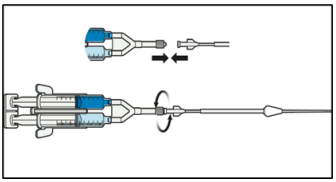


7. Carefully attach the Plunger Cap to the plungers of both syringes while holding the plungers.



NOTE: Avoid dispensing solutions into the Y-Connector. If fluids are dispensed into the Y-Connector, discard and replace the device.

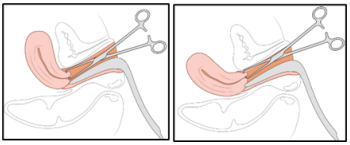
8. Attach the Acorn Catheter to the Juveena® Hydrogel System via the Y-Connector.



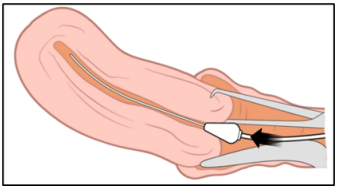
Procedure Instruction

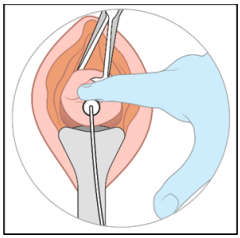
E. Instillation of the Juveena® Hydrogel into the Uterine Cavity

1. Using a vaginal speculum and a tenaculum, position the external cervical os so it can be visualized during catheter insertion.



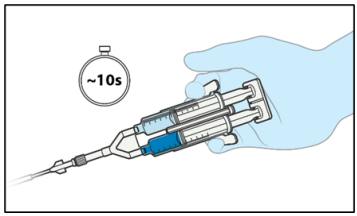
2. With cervix exposed and stabilized with the tenaculum, carefully insert the catheter until the back of the acorn is flush with external cervical os.





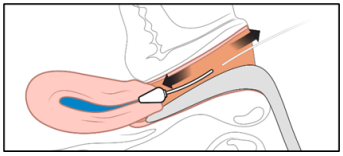
3. While maintaining the acorn position to seal the external cervical os, begin instillation in a continuous manner without pause to prevent clogging. Completely fill the uterine cavity with the hydrogel. Instill the full contents of both syringes.

CAUTION: the gel will form within seconds. Pausing instillation will result in clogging of the Y-Connector and catheter.



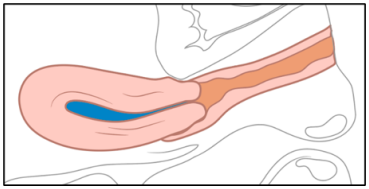
NOTE: In the event of a clog during instillation, discontinue use and replace the Juveena® Hydrogel System and Rejoni Acorn Catheter, as appropriate.

4. When instillation is complete, hold the acorn in place at the external cervical os and withdraw the catheter from the acorn to maintain hydrogel placement during catheter removal.



NOTE: Egress of some blue hydrogel may be seen around the acorn in smaller uterine cavities.

5. Carefully remove the acorn and dispose of all components. The instillation procedure is complete.



NOTE: A maximum of 10mL of the Juveena® Hydrogel System may be used per patient.

Glossary of Symbols:

Symbol	Symbol Title /Description
	**Follow Instructions for Use** / Refer to instruction manual/booklet.
	**Catalogue or Model Number** / Indicates the manufacturer's catalogue number so that the medical device can be identified.
	**Lot Identification** / Indicates the manufacturer's batch code so that the batch or lot can be identified.
	**Sterilized Using Radiation** / Indicates medical device has been sterilized using electron beam radiation
	**Use by** / Indicates the date after which the medical device is not to be used (YYYY-MM-DD).
	**Single Use only** / Indicates medical device that is intended for one use, or for use on a single patient during a single procedure.
	**Storage temperature range** / Indicates range of temperature the medical device can be safely exposed.
	**Single sterile barrier system /** Indicates aseptic presentation technique requires opening by an assistant nurse. (Sterile) Scrub nurses or surgeons must not touch the outer surface of the packaging. Pack must not be placed on sterile surfaces.
	**Single sterile barrier system with protective packaging inside/** Indicates aseptic presentation technique requires opening of the outer packaging by an assistant nurse. Sterile nurses or surgeons must not touch the surface of the outer packaging. The inner layer with the sterile product may be handled by sterile personnel. Product in inner layer can be placed on sterile surfaces.
	**Non-pyrogenic** / indicates that the product is non-pyrogenic.
	**Manufacturer** / Indicates the medical device manufacturer.
Rx **ONLY**	**Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician or licensed practitioner.



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