Healon® EndoCoat Ophthalmic Viscosurgical Device

Z311182 Rev. B
Revision Date: 06/2019
EN

Rx Only

FOR INTRAOCULAR USE AS A SURGICAL AID IN ANTERIOR SEGMENT SURGERY ONLY.

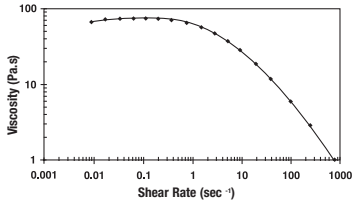
DESCRIPTION

Healon® EndoCoat Ophthalmic Viscosurgical Device (OVD) is a sterile non-pyrogenic solution of highly purified sodium hyaluronate with dispersive rheological properties. Healon® EndoCoat OVD contains 30 mg/ml of sodium hyaluronate. The concentration is adjusted to yield a viscosity of approximately 50,000 centipoise when dissolved in a physiological buffered salt solution. The solution has an osmolality of approximately 320 milliosmoles/kg.

CHARACTERISTICS

Sodium hyaluronate is a linear polysaccharide composed of repeating disaccharides of sodium glucuronate and N-acetylglucosamine found throughout the tissues of the body with high concentrations in the vitreous humor, synovial fluid, and umbilical cord. It has a role in regulating the interactions between adjoining tissues. Sodium hyaluronate can also act as a viscoelastic space filler, maintaining a separation between tissues. Sodium hyaluronate does not interfere with the normal wound healing process. Sodium hyaluronate is also present in the capsular material of certain bacteria. Those bacteria may be cultured by a fermentation process to yield sodium hyaluronate. Sodium hyaluronate extracted and purified from different sources can have different molecular weights but has the same molecular structure. The sodium hyaluronate in Healon® EndoCoat OVD is a highly purified extract of a bacterial fermentation and is tolerated well in the eye. It has an average molecular weight of approximately 800,000 Daltons is non-antigenic (1, 2, 3), and non-pyrogenic.

Rheological Profile of Healon® EndoCoat OVD Measured at 25°C



INDICATIONS

Healon® EndoCoat OVD is an ophthalmic viscoelastic containing 3% sodium hyaluronate indicated for use as a surgical aid in patients undergoing ophthalmic anterior segment procedures including:

- Cataract surgery with an intraocular lens.
- Cataract surgery without an intraocular lens.
- Secondary intraocular lens implantation.

Healon® EndoCoat OVD maintains a deep chamber during anterior segment surgery, aids in tissue manipulation during surgery, enhances visualization during the surgical procedure and protects the corneal endothelium and other ocular tissue. The viscoelasticity of the solution maintains the normal position of the vitreous face and prevents formation of a flat chamber during surgery. It may also be used to coat intraocular lenses and insertion instruments prior to intraocular lens implantation.

CONTRAINDICATIONS

At present, there are no contraindications to the use of Healon® EndoCoat OVD when used as recommended.

WARNINGS

The Healon® EndoCoat OVD Delivery system is not designed or intended to be attached to instruments other than the one provided with the product. Failure to follow the "Directions for Use" may result in cannula detachment.

Mixing of quaternary ammonium salts, such as benzalkonium chloride, with sodium hyaluronate results in the formation of a precipitate. The eye should not be irrigated with any solution containing benzalkonium chloride if Healon® EndoCoat OVD is to be used during surgery.

DIRECTIONS FOR USE

Cataract surgery and intraocular lens (IOL) implantation: Inject Healon® EndoCoat OVD slowly through the cannula into the anterior chamber. The use of Healon® EndoCoat OVD is most effective when the injection is made before phacoemulsification removal of the cataract and before insertion of the IOL. Healon® EndoCoat OVD can also be applied to the IOL before placement. During the procedure, more Healon® EndoCoat OVD can be infused for anterior chamber maintenance or to replace viscoelastic lost during surgery. At the end of the surgical procedure, it is required that Healon® EndoCoat OVD be completely removed from the eye by thoroughly irrigating and aspirating with a sterile irrigation solution. Due to the adherent nature of a dispersive viscoelastic more time and care may be required to remove the viscoelastic completely from the eye.

PRECAUTIONS

CAUTION: Injection of viscoelastics creates pressure in the syringe. To prevent expulsion of the cannula into the eye, ensure that the cannula is securely attached to the fitting on the syringe. Use of the cannula guard is recommended.

CAUTION: The cannula should be fastened securely to the syringe; however, over tightening may cause the hub to weaken and possibly detach from the syringe. Extrusion of a test droplet is recommended prior to entering the eye, and excessive force on the plunger should be avoided.

CAUTION: Do not reuse the cannula. This could release particulate matter. Product and cannula are for single use only. Re-use may cause eye inflammation.

CAUTION: The potential for early and short-term postoperative intraocular pressure (IOP) spikes exists with dispersive OVDs, which potentially require more time and care to remove from the eye. Therefore, it is recommended that Healon® Endocoat OVD be removed from the eye completely by irrigating and aspirating with sterile irrigation solution to reduce the risk of early postoperative IOP spikes.

Observe the usual precautions taken during anterior segment surgery.

Pre-existing glaucoma, the surgery itself, or retained viscoelastic (particularly in patients with compromised trabecular meshwork) can cause increased intraocular pressure after the procedure (4).

The following precautions should be carefully considered:

- The intraocular pressure of postoperative patients should be carefully monitored, particularly in the early post operative period.
- Do not use excessive amounts of Healon® EndoCoat OVD.
- Remove Healon® EndoCoat OVD completely from the anterior chamber at the end of the procedure.
- Corrective therapy should be initiated if the postoperative intraocular pressure rises above safe levels.
- For intraocular use only.
- Store at 2-25°C (36-77°F).
- Protect from freezing.
- Protect from light.
- Use only if solution is clear.
- Avoid trapping air bubbles.
- Contents are sterile when the package is sealed and undamaged.
- Use aseptic technique.
- Do not use in cases of known hypersensitivity to any of the ingredients of this product.
- See product expiration date.

Healon® EndoCoat OVD does not require refrigeration. If refrigerated, Healon® EndoCoat OVD should be allowed to attain room temperature prior to use.

There have been isolated reports of diffuse particulates or haziness appearing after injection of viscoelastics into the eye. While such reports are infrequent and seldom associated with any effects on ocular tissue, the physician should be aware of this occurrence. If observed, the viscoelastic should be removed by irrigation and/or aspiration.

Healon® EndoCoat OVD is derived from microbial fermentation by a purified proprietary process. Although precautions have been taken to make this device protein-free, it may contain trace amounts of protein. The physician should be aware of the potential allergic risks such as postoperative inflammation that can occur with injection of biological materials.

Adverse Reactions

Because sodium hyaluronate is a polysaccharide present in many tissues of the body, it is extremely well tolerated in human eyes. There have been reports of transient postoperative ocular inflammation (oral and/or topical steroid treatments were administered) (5) and transient postoperative increases in intraocular pressure (4) during clinical trials with viscoelastics.

In addition to the above, the following adverse reactions have been reported following the use of sodium hyaluronate in intraocular surgery: inflammation, corneal edema, increased intraocular pressure, secondary glaucoma and corneal decompensation.

All of the adverse reactions described above are potential adverse reactions for Healon® EndoCoat OVD.

Refer to the Clinical Trial Section for more details regarding adverse reactions (i.e. adverse events) that occurred in our study and the incidence rates.

Clinical Trial

Healon® EndoCoat OVD in the 2.25mL configuration was compared to Viscoat® in a randomized, double-masked, multi-center clinical trial between September 10, 2009, and August 11, 2010. Four hundred subjects (200 Healon® EndoCoat OVD and 200 Viscoat® OVD) with cataracts who were otherwise healthy, nonglaucomatous patients who did not receive prophylactic IOP lowering medications were evaluated for safety and effectiveness.

Healon® EndoCoat Ophthalmic Viscosurgical Device

This study was conducted to evaluate the safety and effectiveness of an investigative dispersive ophthalmic viscoelastic under normal use conditions during phacoemulsification cataract surgery and intraocular lens placement as compared to a currently marketed dispersive OVD.

Safety was assessed by two primary endpoints: Cumulative rate of Intraocular Pressure (IOP) spikes ≥30 mm Hg and mean percent change in corneal endothelial cell count (ECC) between the preoperative and three months postoperative visits.

Following surgery, intraocular pressure (IOP) was measured at 6 hours, 24 hours, 7 days, 1 month and 3 months. Study results demonstrate that for the percentage of subjects with an IOP spike defined as IOP ≥30 mm Hg (subjects did not receive IOP lowering medications at the time of surgery), Healon® Endocoat OVD is non-inferior to Viscoat® OVD with regard to the cumulative percentage of subjects with IOP ≥30 mm Hg during the study (p=0.0003, δ=0.13, 90% confidence interval (-1.74, 7.72)).

Operative complications were reported in the safety population for 3% (6/200) of subjects in the Healon® Endocoat OVD group and 8% (16/200) in the Viscoat® OVD group.

Operative Complications
Safety Population

Operative Parameters		Healon EndoCoat N = 200 n	%	Viscoat N = 200 n	%
Surgical Complications	None	194	97.0	184	92.0
	Detached Descemet's membrane	2	1.0	2	1.0
	Iris damage	0	0.0	1	0.5
	Endothelial touch	0	0.0	2	1.0
	Capsule rupture/tear	2	1.0	6*	3.0
	Vitreous bulge or loss	1	0.5	2*†	1.0
	Zonular rupture	0	0.0	1	0.5
	Corneal abrasion	1	0.5	0	0.0
	IOL exchange	0	0.0	2	1.0
	Iris retraction	0	0.0	1	0.5

Safety Population - analysis population consisting of all subjects exposed to an OVD.
* One subject had both a capsular rupture and vitreous bulge. One subject had both a capsulotomy and a vitrectomy.
† One subject had both a capsulotomy and a vitrectomy.

Percent IOP ≥ 30 mmHg
by Viscoelastic Group, Visit and Cumulative
Intent To Treat (ITT) Population*

Visit	VISCOELASTIC GROUP	N	Rate of IOP spikes (%)/ (Number of IOP Spikes)	
6 Hours	Healon® EndoCoat OVD	199	7.5	(15)
	Viscoat® OVD	201	6.1	(12)
	Difference	-	**1.4**	
1 Day	Healon® EndoCoat OVD	199	2.5	(5)
	Viscoat® OVD	201	2.0	(4)
	Difference	-	**0.5**	
1 Week	Healon® EndoCoat OVD	199	1.0	(2)
	Viscoat® OVD	201	1.0	(2)
	Difference	-	**0**	
1 Month	Healon® EndoCoat OVD	199	0	
	Viscoat® OVD	201	0	
	Difference	-	**0**	
3 Month	Healon® EndoCoat OVD	199	0	
	Viscoat® OVD	201	0	
	Difference	-	**0**	
Cumulative*	Healon® EndoCoat OVD	199	10.6	(21)
	Viscoat® OVD	201	7.6	(15)
	Difference	-	**3.0**	**(-1.74, 7.72)****

Intent To Treat (ITT) primary analysis population where missing values were imputed
* Missing values are imputed by MCMC multiple imputation. Therefore, percent IOP ≥30 mmHg rather than number of IOP ≥30 mmHg is reported.
** 90% Confidence interval. Healon® EndoCoat OVD is statistically significantly non-inferior to Viscoat® OVD (p=0.0003).

Post-Operative IOP Spike Rate Over Time
Safety Population*
Healon® EndoCoat OVD

IOP	6 Hours N = 200		1 Day N = 200		1 Week N = 199		1 Month N = 200		3 Months N = 200	
	n	%	n	%	n	%	n	%	n	%
< 30 mmHg	185	92.5	195	97.5	197	98.9	200	100.0	200	100.0
≥30-39 mmHg	11	5.5	4**	2.0	2**	1.0	0	0.0	0	0.0
≥40-49 mmHg	2	1.0	1	0.5	0	0.0	0	0.0	0	0.0
≥ 50-60 mmHg	2	1.0	0	0.0	0	0.0	0	0.0	0	0.0

* In the absence of IOP lowering medication administered at the time of surgery
** One subject experienced an IOP spike one day postoperatively of 38 mmHg and an IOP of 31 mmHg at one week postoperatively off of IOP lowering medications

Post -Operative IOP Spike Rate Over Time
Safety Population*
Viscoat® OVD

IOP	6 Hours N = 198		1 Day N = 200		1 Week N = 199		1 Month N = 198		3 Months N = 199	
	n	%	n	%	n	%	n	%	n	%
< 30 mmHg	186‡	93.9	196‡	98.0	197	99.0	198	100.0	199	100.0
≥30-39 mmHg	10**†	5.1	2†	1.0	1‡	0.5	0	0.0	0	0.0
≥40-49 mmHg	2	1.0	2**	1.0	1**	0.5	0	0.0	0	0.0
≥ 50-60 mmHg	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

* In the absence of IOP lowering medication administered at the time of surgery
** One subject experienced an IOP of 39 mmHg at six hours postoperatively. Although IOP lowering medications and/or treatments were administered, the IOP rose to 41 mmHg at one day postoperatively. The IOP measured 46 mmHg at one week postoperatively off of IOP lowering medications;
† One subject had an IOP of 35 mmHg six hours postoperatively. After IOP lowering medications and/or treatments were administered the IOP measured 32 mmHg at one day postoperatively.
‡ One subject had an IOP of 38 mmHg at 1 week postoperatively, which had been preceded by unmedicated IOPs of 28 mmHg at 6 hours postoperatively and 26 mmHg at 1 day postoperatively.

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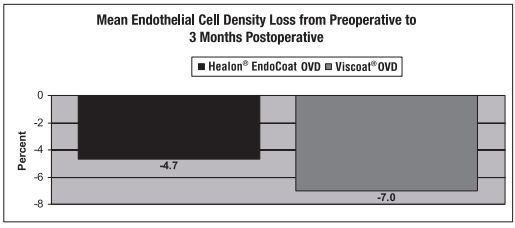
Healon® EndoCoat Ophthalmic Viscosurgical Device

Healon® Endocoat OVD demonstrated non-inferiority compared to Viscoat® OVD in corneal endothelial cell count (ECC) from preoperative to three months postoperative ($p<0.0001$, 1-sided t-test, $\delta = 5\%$). The observed mean percent changes in ECC from preoperative to three months postoperative for Healon® Endocoat OVD and Viscoat® OVD were -4.7% and -7.0%, respectively with a 2.3 percentage point difference (90% CI: (0.23%, 4.33%)).



The distribution of postoperative medical findings/observations was similar between the two study groups and within the range of what would typically be reported. In the early postoperative period, inflammatory cells in the anterior chamber were the most reported form of inflammation for both viscoelastic groups. Reports of inflammatory cells diminished over time to minimal levels by the one-month visit in both viscoelastic groups. Early postoperative incidence rates of corneal, epithelial and stromal edema were low with similar results in both groups, diminishing over time. For other general slit-lamp findings, the majority of subjects in both groups were reported as "none" at all postoperative visits.

Clinical Trial Adverse Events

Safety Population

Thirty nine subjects experienced adverse events in the study. None of the adverse events were considered unanticipated. Ninety-two percent of the adverse events were IOP ≥30 mmHg; incidence of IOP ≥30 mmHg occurred at a rate of 10.5% in the Healon® EndoCoat OVD group, and 7.5% in the Viscoat® OVD group. The three adverse events not related to IOP ≥30 mmHg include: one subject in the Healon® EndoCoat OVD group who developed cystoid macular edema (CME) requiring treatment and two subjects in the Viscoat® OVD group; one who underwent a lens explant in the study eye due to a shorn haptic and another who had an intraocular foreign body removed from the study eye. None of these three events was considered by the investigators to be related to the viscoelastic used.

ADVERSE EVENT	Healon® EndoCoat OVD N = 200		Viscoat® OVD N = 200	
	n	%	n	%
Elevated IOP ≥ 30 mmHg	21*	10. 5	15*	7.5
IOL Exchange	0	0.0	1	0.5
Treatment of CME	1	0.5	0	0.0
Removal of Foreign Body**	0	0.0	1	0.5
Total Subjects Experiencing Adverse Events	**22**		**17**	

* One subject in each group experienced two separate incidences of IOP ≥ 30 mmHg.

** Intraocular foreign body was noted at the one month postoperative visit

Although not included in the primary outcome parameters, the surgical time spent on OVD removal was recorded during the study. A subjective response was requested from surgeons at the end of the case regarding the ease of removal of the viscoelastic (choices were: easy, average, difficult, or hard).

Safety Population
Operative Parameters - Removal of Viscoelastic agent

Viscoelastic Removal		Healon® Endocoat OVD N = 200		Viscoat® OVD N = 200	
Viscoelastic removal time (seconds)	Mean	149.1		133.7	
	SD	37.92		35.21	
	Median	135.0		121.0	
	Min	60		60	
	Max	300		454	
Ease of viscoelastic removal (no. of cases)	Easy	7	3.5%	9	4.5%
	Average	126	63%	142	71%
	Difficult	66	33%	49	24.5%
	Very Difficult	1	0.5%	0	0%

HOW SUPPLIED

Healon® EndoCoat OVD is a sterile, non-pyrogenic preparation supplied in a disposable single-use glass syringe, delivering 0.85 ml of a solution of sodium hyaluronate in a physiological buffered salt solution.

A sterile, single-use 25-gauge, disposable, bent, blunt-tip thin-wall cannula and cannula guard are provided within the package. The cannula sheath should be used to firmly attach the cannula to the syringe. Contents of unopened and undamaged blister package are sterile. Do not use if package is opened or damaged.

Contents

Each ml of Healon® EndoCoat OVD contains:

Ingredient	Contents per ml
sodium hyaluronate	30.00 mg
sodium chloride	5.00 mg
potassium chloride	0.56 mg
calcium chloride	0.36 mg
magnesium chloride	0.22 mg
sodium acetate	2.92 mg
sodium citrate	1.28 mg
sodium phosphate dibasic	0.42 mg
sodium phosphate monobasic	0.06 mg
water for injection	as required

Healon® EndoCoat OVD exhibits an osmolality of approximately 320 mOsm/kg and a pH of 6.8 - 7.6.

Healon® EndoCoat OVD is filter sterilized and aseptically filled. The packaged product is secondarily sterilized using ethylene oxide.

REFERENCES

1. Richter W. Non-immunogenicity of purified hyaluronic acid preparations tested by passive cutaneous anaphylaxis. Int Arch Allergy 1974; 47:211.
2. Richter, W. Ryde EM, Zetterstrom EO. Non-immunogenicity of a purified sodium hyaluronate preparation in man. Int Arch Appl Immunol 1979; 59:45.
3. Lifecore Biomedical document of antigenicity studies.
4. Miller D, Stegmann R. The use of Healon® in intraocular lens implantation. Int Ophthalmol clinics 1982; 22:177.
5. Pruett RC, Schepens CL, Swann DA. Hyaluronic acid vitreous substitute. A six year clinical evaluation. Arch Ophthalmol 1979; 87:699.

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

Healon® EndoCoat Ophthalmic Viscosurgical Device

SYMBOLS USED ON STERILE PACKAGING

SYMBOLS	ENGLISH
	Consult Instructions For Use
	Caution
	Do Not Use if Package is Damaged
	Do Not Reuse
STERILE A	Sterile using Aseptic Processing Techniques
STERILE EO	Packaging and Cannula Sterilized using Ethylene Oxide
REF	Catalogue Number
LOT	Lot Number
	USE BY (YYYY-MM-DD: year-month-day)
	Protect From Light
	Protect From Freezing
	Temperature Limitation
	Manufacturer
EC REP	Authorised Representative in the European Community
	Date of Manufacture (YYYY-MM-DD: year-month-day)

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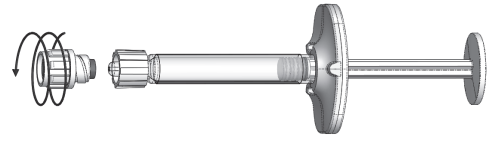
CE 0344

EC REP AMO Ireland
Block B
Liffey Valley Office Campus
Quarryvale, Co. Dublin, Ireland

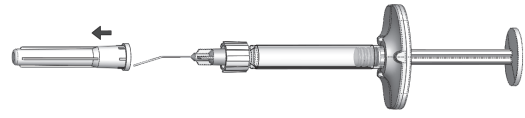
Product of USA

1 Remove plastic tip cap from syringe tip.



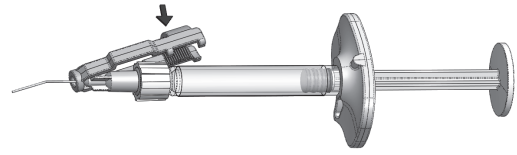
2 Thread the 25 gauge cannula onto the syringe and confirm that it is firmly seated.

3 Remove the plastic sheath from the cannula by pulling it away in a straight motion. Ensure that cannula remains fully seated to syringe.

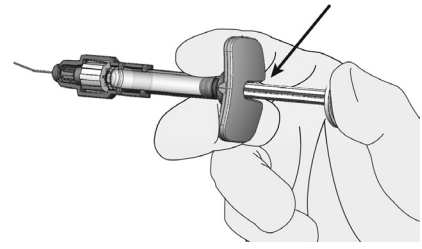


4 Guide the cannula needle through the opening of the cannula guard provided until the cannula guard is fully seated against the cannula hub.

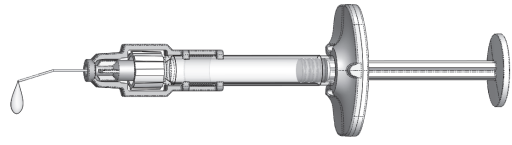
Click the cannula guard in place around the syringe.



5 Syringe Orientation: Hold the syringe with the opening of the finger grip (backstop) facing the palm.
Rotate syringe body within the finger grip to achieve desired cannula positioning.



6 Check proper function by holding the syringe barrel and gently depressing the plunger rod until the OVD appears at the cannula tip.



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