

Table 5. Number of patients with iritis. All randomized qualified patients.

	Visit and group			
	Op + 24 hours		Op + 7 days	
	Healon5 N=187	Healon N=172	Healon5 N=187	Healon N=172
Iritis				
Not assessed	0	0	1*	0
None	107	95	121	109
Slight	54	49	63	60
Moderate	26	27	1	2
Severe	0	1	0	0

* For patient 114 iritis was not assessed at visit 5, 7 ± 2 days after surgery.

Two Healon5 OVD events were scored as possibly device related by the investigators.

Table 6. Adverse Events. Number of patients in whom a medical event occurred at least once. All randomized qualified patients.

Body system	Preferred term	Group				Total	
		Healon5 N=187		Healon N=172		N	%
Vision	CONJUNCTIVAL HEMORRHAGE	2	1.1	1	0.6	3	0.8
	CORNEAL OPACITY	0	0	1	0.6	1	0.3
	EYE INFECTION	0	0	1	0.6	1	0.3
	EYE PAIN	0	0	1	0.6	1	0.3
	INCREASED INTRAOCULAR PRESSURE	4	2.1	4	2.3	8	2.2

The difference in percent change in endothelial cell counts between the Healon5 OVD and the Healon OVD has been investigated in another clinical study. The endothelial cell count evaluation included 81 patients in the Healon5 OVD group and 78 in the Healon OVD group. The mean age in the Healon5 OVD group was 69.9 years and in the Healon OVD group 68.9 years.

No difference was observed between the treatment groups with regard to the change from pre-operative values to the values determined at 3 months after surgery. The percentage cell loss in the Healon5 OVD group was 9.4 and in the Healon OVD group 11.2%.

Table 7. Endothelial cell counts, changes and percentage change in endothelial cell counts from pre-surgery at 3 months.

	N	Visit	
		Visit 1 (Pre-op)	Visit 7 (Op + 3 months)
Healon5® OVD			
Endothelial cell counts	81	2548 ± 292	2314 ± 380
Change from pre-surgery			-243 ± 283
Percentage changes from Pre-surgery			-9.45 ± 10.67
Healon® OVD			
Endothelial cell counts	78	2454 ± 321	2193 ± 407
Change from pre-surgery			-276 ± 295
Percentage changes from Pre-surgery			-11.20 ± 11.50

How Supplied

The Healon5 OVD is a sterile, non-pyrogenic, viscoelastic preparation supplied in disposable 0.6 mL glass syringe. Each mL of the Healon5 OVD contains:

- 23 mg sodium hyaluronate 5000
- 8.5 mg sodium chloride
- 0.28 mg disodium hydrogen phosphate dihydrate
- 0.04 mg sodium dihydrogen phosphate dihydrate
- q.s. water for injection

The Healon5 OVD syringes are terminally steam sterilized and aseptically packaged.

A sterile single-use, 25 gauge cannula is included with each syringe.

Preparation and Storage

Refrigerated Healon5 OVD should be held at room temperature for approximately 30 minutes before use. Store between 2° to 8°C (36° to 46°F). Protect from freezing and exposure to light.

Definition of symbols on cannula, syringe-, blister label and carton.

	Caution, see instructions for use
	See instructions for use
	Do not reuse
	Protect from light
	Do not use if the packaging has been opened or damaged
	Protect from freezing
	Temperature limitation
	Sterilized using steam
	Sterilized by ethylene oxide
	Manufacturer
	Batch code
	Use by (YYYY-MM : year month)
	Latex Free
	Catalogue number

References

- Richter, W., Ryde, M. & Zetterström, O. Nonimmunogenicity of a purified sodium hyaluronate preparation in man. *Int Arch Appl Immun* 59:45-48 (1979)
- Balazs, E.A.: Ultrapure hyaluronic acid and the use thereof. U.S. patent 4,141,973 (1979)
- Richter, W.: Non-immunogenicity of purified hyaluronic acid preparations tested by passive cutaneous anaphylaxis. *Int Arch All* 47 (1974) p 211-217.
- Pharmacia & Upjohn Anterior chamber depth maintenance capacity of sodium hyaluronate 5000, 23 mg/mL, during phacoemulsification in pig cadaver eyes. Data on file.
- Holst A, Osterling L. An open, randomized, parallel group, phase III study of Healon5® OVD compared to Healon® OVD during cataract surgery with a 7 day follow up period. Pharmacia&Upjohn Report c0025536
- Lundberg K, Osterling L. A double-blind, randomized, parallel group study evaluating the safety of a new viscoelastic agent UPG-96 (Healon5® OVD), compared to Healon® OVD in the phacoemulsification with intraocular lens implantation. Pharmacia&Upjohn Report c0002131

Rx only

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Healon5®

Sodium Hyaluronate

LATEX FREE

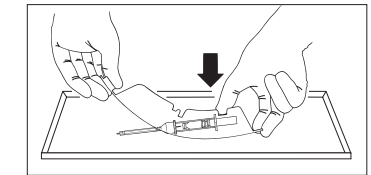
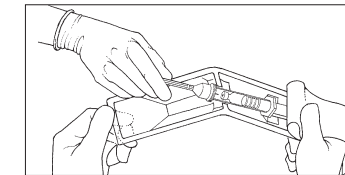
Instructions

Sterile opening technique

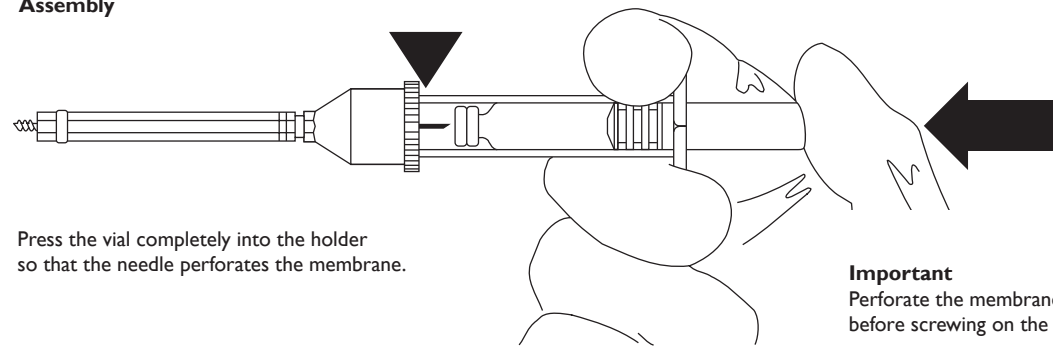
Tear off the paper covering.

Bend the plastic backwards at the central indentation so as to fully expose the white plastic rod.

Dislodge syringe and place onto sterile field.

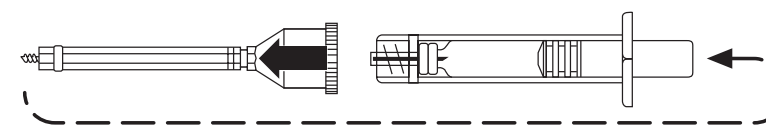


Assembly

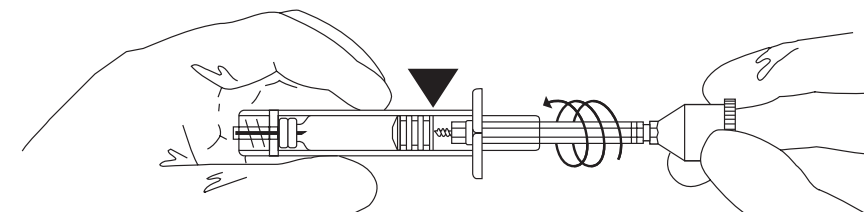


Press the vial completely into the holder so that the needle perforates the membrane.

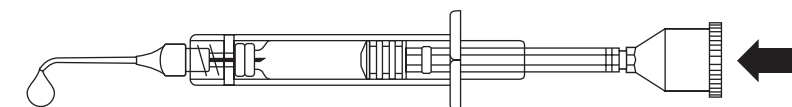
Important
Perforate the membrane before screwing on the plastic rod.



Remove the plastic rod.



Screw the plastic rod into the blue plunger.



Connect the cannula and check for proper function.

Store at 2 to 8°C (36 to 46°F).

For single use only



Product information

Description

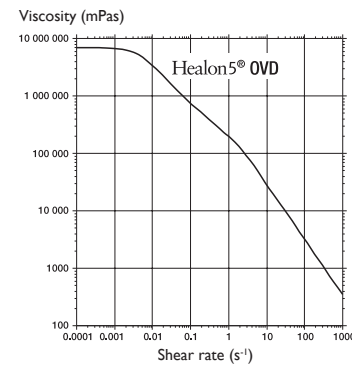
The Healon5® Ophthalmic Viscosurgical Device (OVD) is a sterile, non-pyrogenic, transparent viscoelastic preparation of a highly purified, noninflammatory, high molecular weight fraction (average molecular weight 4 million) of sodium hyaluronate. The Healon5 OVD contains 23 mg/mL of sodium hyaluronate 5000, dissolved in repeating disaccharide units of N-acetylglucosamine and sodium glucuronate linked by glycosidic bonds.

Sodium hyaluronate is a physiological substance that is widely distributed in the extracellular matrix of connective tissues in both animals and man. For example, it is present in the vitreous and aqueous humor of the eye, the synovial fluid, the skin, and the umbilical cord. Sodium hyaluronates derived from various human or animal tissues do not differ chemically.

The fraction of sodium hyaluronate in the Healon5 OVD is reported to be nonantigenic^{1,3} and does not cause inflammatory² or foreign body reactions.

The graph below represents the flow curve (shear viscosity versus shear rate).

The viscosity of the Healon5 OVD at rest (at zero shear rate) is about 7 million mPas, a viscosity higher than the Healon OVD and the Healon GV OVD. At high shear rates, such as during injection, the viscosity of the Healon5 OVD decreases dramatically due to high pseudoplasticity, facilitating injection through a 25G cannula.



Indications

The Healon5 OVD is intended for use in anterior segment ophthalmic surgical procedures of the human eye. The Healon5 OVD is designed to create and maintain a deep anterior chamber which facilitates manipulation inside the eye with reduced trauma to the corneal endothelium and other ocular tissues.⁴ The Healon5 OVD can also be used to efficiently separate and control ocular tissues. The Healon5 OVD is not designed to have any pharmacological effect.

Contraindications

There are no known contraindications to the use of the Healon5 OVD when used as recommended.

Precautions

Precautions normally considered during ophthalmic surgical procedures should be taken.

Special care should be taken to ensure complete removal of the Healon5 OVD from the entire eye including behind the lens and the chamber angles. Complete removal of the Healon5 OVD is important to avoid intraocular pressure peaks postoperatively. Due to the greater viscosity and higher concentration of sodium hyaluronate in the Healon5 OVD, the rise in the postoperative intraocular pressure may be higher with the Healon5 OVD than if the same volume of other sodium hyaluronate viscoelastic products, with lower zero shear viscosity, is left in the anterior segment of the eye.

LATEX FREE

Before initiating phacoemulsification, use irrigation/aspiration to create a fluid-filled space above the lens. This reduces the risk of initial visco-occlusion of the phaco tip or the irrigation line which could cause phaco tip heating.

Pre-existing glaucoma, other causes of compromised outflow, higher preoperative intraocular pressure and complications in surgical procedures may also lead to increased intraocular pressure; consequently, extra care should be taken in patients with these conditions. Prophylactic pressure-lowering treatment should always be considered and especially in cases where the Healon5 OVD has to be left in the eye for clinical reasons.

Both the Rock'n Roll technique and the "Behind the Lens" or the Two Compartment Technique (TCT) were evaluated during the clinical trial. The table below reflects IOPs ≥30 mmHg at 5 hours postoperatively in association with removal technique.

Table 1. Patients with IOP ≥30 mmHg at 5 Hour Visit by Removal Technique

		Healon5 N=187	Healon N=172
Rock'n Roll	≥30	7	6
Behind-the-Lens (TCT)	≥30	3	1
Combination of 1 and 2	≥30	11	9
Other	≥30	0	2

As a result of clinical experience, the following removal technique (TCT) is recommended to ensure efficient removal of the Healon5 OVD:

Use a standard I/A tip, 0.3 mm, with effectual flow of 20-25 ml/min and vacuum of 250-300 mmHg with a potential maximum setting at 500 mmHg. When using a machine with a peristaltic pump, use the upper limits of the suggested settings. When using a Venturi pump use the lower limits of the suggested settings. Bottle height should be 60-70 cm above eye level.

1. Start the removal directly after the IOL implantation, while the anterior chamber is still filled with the Healon5 OVD and before the IOL has been centered. Go behind the IOL optic without engaging the flow of the I/A tip (port up) and then start flow. Remove the Healon5 OVD from the capsular bag first and ensure that the lens has adequately centered. During removal of the Healon5 OVD from the capsular bag, the continuous flow of irrigation fluid keeps the bag inflated and reduces the risk of aspirating the capsular bag. While maintaining continuous flow remove the tip from behind the optic and place it on top of the optic.
2. Continue the removal by circling the I/A tip at the iris plane, or on the optic surface, then make an additional sweep in the anterior chamber paying particular attention to the angles.

An alternative technique to remove the Healon5 OVD is to create maximum turbulence to make the Healon5 OVD fracture into large pieces. This can be accomplished by using the Rock'n Roll technique (described below) with standard I/A tip, 0.3 mm, with high settings; flow rates should be 25-30 ml/min and vacuum 350-500 mmHg, depending on the type of pump. If a peristaltic pump is used, the vacuum should be set towards the higher limit.

If a venturi pump is used, the vacuum should be set towards the lower limit. Bottle height should be 60-70 cm above eye level. Today's phaco machines often use linear control. The suggested machine settings can only be achieved if the surgeon operates the phaco machine with fully depressed foot pedal.

1. Start by circling the hand piece in the anterior segment at iris plane.
2. Gently rest the I/A piece on the anterior surface of the optic. Press on the IOL optic on one side and rotate the I/A hand piece directing the flow into the bag. Direct the hand piece port towards the equator of the capsular bag and stay in this position for a few seconds and then repeat on the other side of the IOL optic until the Healon5 OVD is completely removed. Finally, sweep the anterior chamber including the angles and repeat step 2 if necessary.

The Healon5 OVD is a highly purified fraction extracted from avian tissues which may contain minute amounts of protein. The potential risks associated with the injection of biological material should be considered.

Express a small amount of the Healon5 OVD from the syringe prior to use and carefully examine it during use to avoid injecting minute rubber particles which may be released when the syringe diaphragm is punctured.

Sodium hyaluronate solution may appear cloudy or form precipitates when it is injected. In-vitro studies have shown incompatibility, resulting in opalescence, between sodium hyaluronate and solutions containing cationic components, e.g., detergents and benzalkonium chloride.

Reprocessed cannulas should not be used.

Do not use if the blister package has been damaged.

Do not resterilize.

The Healon5 OVD is for single use.

Adverse Events

Increased intraocular pressure has been reported after use of sodium hyaluronate solutions.

Increased intraocular pressure is likely to occur if the Healon5 OVD is not removed as completely as possible. Clinical judgment concerning the use of this product should be considered in cases where thorough removal may not be possible. The precautions noted above should be taken to manage any increased postoperative intraocular pressure and to reduce the likelihood of occurrence of related postoperative complications such as optic neuropathy, pupillary atonia and dilation, and iris atrophy.

Rarely, postoperative inflammatory reactions (iritis, hypopyon, endophthalmitis) following the use of sodium hyaluronate, as well as incidents of corneal edema and corneal decompensation, have been reported. Their relationship to sodium hyaluronate has not been established.

CLINICAL TRIALS 5⁶

A clinical trial of the Healon5 OVD was initiated on August 23rd, 1999. A total of 359 patients were included. 187 patients with a mean age of 74.1 years were randomized into the Healon5 OVD group and 172 patients with a mean age of 73.2 years into the Healon OVD group.

The intraocular pressure (IOP) was assessed at 5 hours after surgery, since the expected IOP peak time period is 4 – 6 hours after surgery. The IOP was measured also at 24 hours and 7 days. No anti-glaucoma medication was permitted until after the 5-hour IOP assessment.

Eleven percent of the Healon5 OVD patients and 10 % of the Healon OVD patients experienced IOP spikes ≥30 mmHg at 5 hours postoperatively.

Table 2. Number of Patients in IOP categories per visits. All randomized qualified patients.

Group	IOP	Visit			
		Pre-surgery	Op + 5 hours	Op + 24 hours	Op + 7 days
Healon5 N=187	0 - 19	164	87	117	162
	20 - 29	23	75	61	23
	30 - 39	0	16	7	1
	40 - 49	0	5	0	0
	50 - 59	0	0	1	0
	60 - 69	0	0	1	0
Healon N=172	0 - 19	161	92	122	154
	20 - 29	11	62	43	17
	30 - 39	0	13	7	0
	40 - 49	0	3	0	0
	50 - 59	0	1	0	0
	60 - 69	0	1	0	0

There was no difference seen between the two groups with regard to the mean IOP at 5 hours after surgery and no difference in mean change. The increase was of the same magnitude in both groups. At 7 days postoperatively, the mean IOP was at pre-operative levels in both study groups.

Table 3. IOP (mmHg) during the study. All randomized qualified patients.

Group	IOP		Visit			
			Pre-surgery	Op + 5 hours	Op + 24 hours	Op + 7 days
Healon5 N=187	IOP	MEAN	15.8	21.2	18.5	15.3
		STD	2.9	7.2	6.1	3.7
		MIN	10	9	8	6
		MAX	23	46	60	30
	Change IOP from preop	N	187	183	187	186
		MEAN	0.0	5.3	2.7	-0.5
		STD	0.0	6.7	6.2	3.6
		MIN	0	-7	-9	-9
		MAX	0	29	47	12
		N	187	183	187	186
					Cont.	
Healon N=172	IOP	MEAN	15.6	20.8	17.9	15.2
		STD	2.7	7.7	4.7	3.1
		MIN	8	8	7	8
		MAX	24	65	37	26
	Change IOP from preop	N	172	172	172	171
		MEAN	0.0	5.2	2.3	-0.4
		STD	0.0	7.2	4.9	2.9
		MIN	0	-8	-10	-9
		MAX	0	46	22	10
		N	172	172	172	171

The specified complications were similar for both groups. All of the complications are commonly seen after cataract surgery. Blurred vision, scratchy sensation, foreign body sensation, itching, burning, tenderness, corneal edema, represented most of the complications recorded in both groups.

Table 4. Number of patients with complications related to surgery. All randomized qualified patients.

Complications related to surgery	Visit and group					
	Healon5 N=183	Healon N=172	Healon5 N=187	Healon N=172	Healon5 N=186	Healon N=171
Missing	0	0	0	0	1*	0
No	166	150	176	153	179	152
Yes	17	22	11	19	6	19

*For patient 341 complications related to surgery at visit 5 had not been recorded.

Iritis was equally distributed between the two groups.