

**APPENDIX 5**

**PHAKIC IOL LABELING  
(ARTISIAN<sup>®</sup> PHAKIC INTRAOCULAR  
LENS, DIRECTIONS FOR USE)**

# ARTISAN® Phakic Intraocular Lens

## Directions for Use

**CAUTION:** Federal Law restricts this device to sale by or on the order of a physician.

**Description**

OPHTEC's ARTISAN® Phakic Intraocular Lenses (IOLs) are single-piece lenses manufactured from Perspex CQ UV ultraviolet light absorbing polymethylmethacrylate (PMMA) with a refractive index of 1.49, which are designed for implantation into the anterior chamber of the phakic human eye for the treatment of myopia. The lenses are affixed to the anterior mid-periphery of the iris stroma by two iridoplastic bridges with enclavation mechanisms. The optic portion of the lens is available in a 5.0 mm or 6.0 mm diameter, with a convex-concave configuration. The 5.0 mm lens is available in a diopter range of -5 to -20 D. The 6.0 mm lens is available in a diopter range of -5 to -15 D. The optic carrier is elliptical in shape and has an overall length of 8.5 mm with a slight anterior vault. One fixation (enclavation) arm mechanism is located on each side of the two peripheral supports.

**Indications for Use**

ARTISAN® Phakic Intraocular Lenses (IOLs) are indicated for:

- the reduction or elimination of myopia in adults with myopia ranging from -5 D to -20 D with less than or equal to 2.5 D of astigmatism at the spectacle plane and whose eyes have an anterior chamber depth greater than or equal to 3.2 millimeters; and
- patients with documented stability of manifest refraction for the prior 6 months, as demonstrated by a spherical equivalent change of less than 0.50 D.

**Contraindications**

The ARTISAN® Phakic IOL is contraindicated in patients:

- Who are less than 21 years old
- With an anterior chamber depth (ACD) less than 3.2 mm
- With an abnormal iris, such as peaked pupil or elevated iris margin
- Who are pregnant and nursing
- Who do not meet the minimum endothelial cell density

**Endothelial Cell Density**

Age	Minimum endothelial cell density
21-25	3550 cells/mm <sup>2</sup>
26-30	3175 cells/mm <sup>2</sup>
31-35	2825 cells/mm <sup>2</sup>
36-40	2500 cells/mm <sup>2</sup>
41-45	2225 cells/mm <sup>2</sup>
> 45	2000 cells/mm <sup>2</sup>

The table indicates the minimum endothelial cell density (ECD) per age group at time of implantation. This table was developed using a rate of 2.31% (the upper 90% confidence interval of the average cell loss for eyes with ACDs of 3.2 mm or greater.) It sets minimum endothelial cell density criteria as a function of age that should result in at least 1000 cells/mm<sup>2</sup> at 75 years of age. The patient's ECD should be monitored periodically at the physician's discretion.

**Warnings**

1. Do not resterilize this intraocular lens by any method. (See Returned Lens Policy.)
2. Do not store lenses at temperatures over 45°C (113°F).
3. Surgical difficulties at the time of intraocular lens implantation, which might increase the potential for complications (e.g. persistent bleeding, significant vitreous prolapse or loss).
4. The effectiveness of ultraviolet light absorbing lenses in reducing the incidence of retinal disorders has not been established.
5. The long-term effect to the corneal endothelial cells has not been established.
6. The relationship between the ARTISAN® Phakic IOL and future lens opacities and retinal detachment is undetermined.
7. The effect of the ARTISAN® Phakic IOL on the future risk of glaucoma is unknown because its effects on the anterior chamber angle were not analyzed in the clinical trial. Approximately 1% of the subjects had elevated eye pressure that required glaucoma medication.
8. The long-term effect to the corneal endothelial cells has not been established.
9. The occurrence of lens opacities in the future is unknown.

**Precautions**

1. Prior to surgery, the surgeon must provide prospective patients with a copy of the patient information brochure for this product and inform these patients of the possible benefits and complications associated with the use of this device.
2. A high level of surgical skill and training specific to iris-fixed IOLs is required for lens implantation.
3. One or more iridotomies/iridectomies should be performed to reduce risk of pupillary block.
4. A cohesive high molecular weight viscoelastic is recommended for corneal protection and complete removal is recommended to reduce the chance of post-op intraocular pressure (IOP) spikes. Low molecular weight non-cohesive viscoelastics should not be used.
5. Patients with any of the following conditions may not be suitable candidates for this intraocular lens because the lens may exacerbate an existing

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condition or may interfere with diagnosis or treatment of a condition or may pose an unreasonable risk to the patient's eyesight:

- a. Abnormality of the iris or ocular structure that would preclude fixation, such as aniridia, hemi-iridectomy, severe iris atrophy, coloboma, or microphthalmos.
- b. Congenital bilateral cataracts.
- c. Recurrent anterior or posterior segment inflammation.
- d. Patients in whom the intraocular lens may interfere with the ability to observe, diagnose or treat posterior segment diseases.
- e. Previous history of retinal detachment.
- f.
- g. Patients with only one eye with potentially good vision.
- h. Glaucoma.
- i. Corneal endothelial dystrophy.
- j. Proliferative diabetic retinopathy.

6. The long-term effects of intraocular lens implantation have not been determined. Therefore, physicians should continue to monitor implant patients postoperatively on a regular basis. Annual exams are recommended.
7. Elevated intraocular pressure has been reported occasionally in patients who received lens implants. The intraocular pressure of patients should be monitored postoperatively.
8. Trauma is a risk factor for IOL dislocation.
9. Visual acuity could be diminished in situations where there is low level lighting.
10. When pupil size is greater than optic size, there may be visual aberrations.

### Adverse Events and Complications

A total of 662 subjects were evaluated in the clinical trial to determine the safety of the ARTISAN® Phakic IOL.

The complications experienced during the clinical trial of the ARTISAN® Phakic IOL include (in order of frequency): Hyphema (cumulative) (0.2%), retinal detachment (cumulative) (0.6%), IOL dislocation (0.8%) and surgical reintervention (4.2%). No incidences of macular edema, endophthalmitis, hypopyon, or persistent corneal edema were reported during the study.

Incidences of complications (compared with the FDA Grid for cataract extraction and posterior chamber IOL implantation) and incidences of surgical reinerventions are shown in the following table.

Adverse Event	Cumulative % (n/N)	FDA Grid %	Persistent (3 Years) % (n/N)	FDA Grid %
Endophthalmitis	0.0 (0/662)	0.1	-	-
Hyphema	0.2 (1/662)	2.2	-	-
Hypopyon	0.0 (0/662)	0.3	-	-
IOL Dislocation	0.8 (5/662)*	0.1	-	-
Cystoid Macular Edema	0.0 (0/662)	3.0	0.0 (0/232)	0.5

Pupillary Block	0.0 (0/662)	0.1	-	-
Retinal Detachment	0.6 (4/662) <sup>†</sup>	0.3	-	-
Surgical Reintervention	4.2 (28/662)	0.8	-	-
Corneal Edema	-	-	0.0 (0/232)	0.3
Iritis	0.5(3/662) <sup>‡</sup>	-	0.0 (0/232)	0.3
Raised IOP Requiring Treatment	-	-	0.0 (0/232)	0.4
<b>Surgical Treatments Not Monitored in the FDA Grid</b>				
Preventative Lens Repositioning	2.1 (14/662)	-	-	-
Refractive Procedures**	2.6 (17/662)	-	-	-
Nd:Yag Peripheral Iridotomy	3.0 (20/662)	-	-	-
Aqueous Release	1.8 (12/662)	-	-	-
Resuture Wound Leak	1.2 (8/662)	-	-	-

\*Four events due to inadequate surgical fixation; one event due to blunt trauma

<sup>‡</sup>There is no FDA Grid value for cumulative iritis

<sup>†</sup>Comparison should be made to literature for retinal detachment rates for high myopes:

- Retinal detachment rates increase with increasing myopia<sup>1</sup>  
The risk of retinal detachment within one year of implantation of this device is 0.6%. The risk of retinal detachment for high myopes following implantation is more than 10 times the risk without surgery, i.e., greater than 10-fold the background rate of retinal detachment for high myopes (greater than minus 3 diopters).
- 5.0% in myopic eyes > 6 D<sup>2</sup>
- 0.8% to 7.5% in pseudophakic eyes with high axial myopia<sup>3</sup>

<sup>1</sup> Ogawa, A and Tanaka, M. The relationship between refractive errors and retinal detachment, Jpn J. Ophthalmology 32:310; 1988.

<sup>2</sup> Dellone-Larkin G, Dellone CA. Retinal detachment. Available at <http://www.emedicine.com/emerg/topic504.htm>. Accessed January 13, 2004.

<sup>3</sup> Jacobi, F and Hessemer, V. Pseudophakic retinal detachment in high axial myopia, J. Cat. Refract Surg 23:1095, 1997.

\*\*Refractive procedures include: LASIK (11/17); AK (3/17); LRI (2/17) and PRK (1/17).

Surgical reinterventions (see table below) were not shown to have an impact on safety or efficacy.

Adverse Event	n	%*
Lens Explant	10	1.5%
High Myopia/Age Related Cataract	0	
Inflammatory Response	3	
Trauma	4	
Patient Anxiety	1	
Patient Not Satisfied	1	
Pupil Larger than Lens Optic	1	
Lens Exchange	9	1.4%
Pupil Calculation Error	6	
Pupil Larger than Lens Optic	2	
Inadequate Lens Fixation	1	
Lens Reattachment	5	0.7%
Trauma	1	
Inadequate Lens Fixation	4	
Retinal Repair	4	0.6%
Retinal Detachment	4	
<b>Total</b>	<b>28</b>	<b>4.2%</b>

\* All Core Subjects N=662

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### Other Complications

Eyes with brown irides were found to have significantly less pigment dispersion (15.3%) compared to eyes with non-brown irides (25.2%). However, eyes with brown irides had similar rates of IOP spikes greater than 30 mmHg (5.2%) compared to eyes with non-brown irides (3.9%). The interaction between pigment dispersion and brown irides was found to be a significant predictor of IOP spikes. Eyes with brown irides and pigment dispersion had a statistically significant (Fisher's Exact Test,  $p=0.02$ ) higher rate of IOP spikes (11.7%) than eyes with non-brown irides and pigment dispersion (3.1%).

### Clinical Study Results

The ARTISAN® Phakic IOL was evaluated in a prospective, nonrandomized study of 662 subjects, 493 of which were followed for one year and 232 followed for three years.

The 662 subject Cohort population in the clinical trial consisted of 64.5% females (427/662) and 35.5% males (235/662). 85.0% were Caucasian, 3.2% were Black, 4.1 % were Hispanic and 6.2% were Asian. The mean age was 39.6 years.

### Visual Acuity

The postoperative results demonstrated that the ARTISAN® Phakic IOL provides correction for high myopia. The visual acuities at one and three years are described in the following tables:

UCDVA=Uncorrected Distance Visual Acuity, Snellen		
Where emmetropia was the goal (+/-0.50D) and Preop Best Corrected Visual Acuity (BCVA) better than or equal to 20/20		
	1 yr	3 yr
N	204	88
20/20 or better	47.1%	44.3%
20/40 or better	93.6%	92.0%
20/80 or better	100.0%	97.7%
worse than 20/80	0.0%	2.3%

BCDVA=Best Corrected Distance Visual Acuity, Snellen		
Eyes with preoperative BCVA 20/20 or better		
	1 yr	3 yr
N	288	127
20/20 or better	95.1%	95.3%
20/40 or better	100.0%	100.0%
20/80 or better	100.0%	100.0%
worse than 20/80	0.0%	0.0%

### Predictability of refraction

The refraction was predictable, with 91.5% of patients achieving  $\pm 1.0$  D from target at the one-year examination.

Spherical Equivalence (Target Variance) Distribution:		
	1 yr	3 yr
N	492	226
Plano to +/- 0.5D	72.0%	71.7%
Plano to +/- 1.0D	94.5%	94.7%

### Stability of refraction

The refraction was stable, with 95.9% of patients achieving less than +/- 1.0 D of shift at 3 years.

Manifest Refraction Spherical Equivalence (MRSE) Change between visits			
	6 mo - 1 yr	1 yr - 2 yr	2 yr - 3 yr
N	485	349	215
+/- 0.5D	82.9%	85.4%	82.5%
+/- 1.0D	97.1%	97.7%	95.9%
+/- 2.0D	99.6%	99.7%	99.5%
>2.0D	0.4%	0.3%	0.5%

### Endothelial Cell Density

The analysis of the change in endothelial cell (EC) density indicated that the EC density remained relatively constant over the three-year study period in relation to normal endothelial cell loss.

An endothelial cell density substudy was performed using a single reading center to minimize standard deviations inherent in this test method. For this subset of 215 subjects (315 eyes), a percent change from baseline to three years of -4.76% (SD=7.8%) was found. This result is consistent with expected normal endothelial cell loss of 1.5% to 2.0% per year. No statistically significant differences in the percent change between consecutive study intervals were found. Covariate analyses including age, anterior chamber depth, lens model, and IOP showed no significant correlations.

Mean EC density results for a consistent cohort group of 57 eyes with useable data available at postop visits are shown in the following table:

Visit	Mean	Standard Deviation	Standard Error	95% Confidence Limits	
PreOp	2818.33	425.01	56.29	2708.00	2928.67
6 Months	2812.86	465.79	61.70	2691.94	2933.78
1 Year	2768.25	460.42	60.98	2648.72	2887.77
2 Years	2760.26	478.54	63.38	2636.03	2884.50
3 Years	2692.98	478.64	63.40	2568.73	2817.24

The available 3-year data from the clinical study indicates a continual steady loss of endothelial cells of -1.8% per year and this rate has not been established as safe. If endothelial cell loss continues at the rate of 1.8% per year, 39% of patients are expected to lose 50% of their corneal endothelial cells within 25 years of implantation. The long-term effect

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on the cornea's health of a 50% loss in corneal endothelial cells is unknown.

The following table shows the predicted endothelial cell loss for the estimated proportion of patients based on percent loss and time from implantation.

Percent Loss	Time from Implantation						
	10	20	30	40	50	60	70
10	48	34	22	13	7	3	1
20	57	46	36	26	18	12	8
30	63	54	44	35	27	20	14
40	67	59	50	42	34	26	20
50	71	63	55	47	39	31	24
60	74	67	60	52	44	36	29
70	77	71	63	56	48	40	32
80	80	74	67	59	51	43	36
90	82	76	70	63	55	47	39
100	84	79	73	66	58	50	42
110	86	81	75	68	61	53	44
120	88	84	78	71	64	55	47

### Optical Visual Symptoms

The following table shows the postoperative outcomes by proportion as compared to preoperative levels for glare, halos and starbursts, etc., stratified by the mesopic pupil sizes measured preoperatively.

Optical Visual Symptom	Pupil Size	Questionnaire Responses		
		Subjects with no change in symptoms preop to postop	Subjects with change in symptoms preop to postop	
			Preop NO, Postop YES	Preop YES, Postop NO
Glare	All	73.6%	13.5%	12.9%
	<4.5 mm	70.4%	14.3%	15.3%
	>4.5 to <5.5 mm	71.6%	13.4%	15.1%
	>5.5 mm	76.3%	16.8% (p=0.04) <sup>†</sup>	6.9%
Starbursts	All	78.5%	11.8%	9.7%
	<4.5 mm	77.8%	12.1%	10.1%
	>4.5 to <5.5 mm	74.5%	16.3%	9.3%
	>5.5 mm	81.2%	10.9%	7.9%
Halos	All	72.0%	18.2% (p=0.002) <sup>†</sup>	9.8%
	<4.5 mm	72.8%	17.2%	10.1%
	>4.5 to <5.5 mm	69.2%	19.2%	11.6%
	>5.5 mm	72.2%	23.8% (p<0.001) <sup>†</sup>	4.0%

\*412 subjects completed the questionnaire, data presented for those subjects that answered nighttime symptom questions; pupil size groups: <4.5 mm (n=99), >4.5 to 5.5 mm (n=172), >5.5 mm (n=101).

<sup>†</sup> Statistically significant (McNemar's Test) for those subjects reporting a change in symptom occurrence preoperatively to postoperatively

### Additional Outcome Data Including Bilateral Eyes

The following table stratifies the predictability of intended refraction for ± 0.5 and ± 1.0 D by lens power for all eyes implanted (662 subjects, 478 bilaterally implanted).

Lens Group	Exam Interval	N	MRSE vs. Intended Target		
			± 0.5 D	± 1.0 D	± 2.0 D
All Diopter Powers	1-6 Day	1037	58.0%	84.4%	92.8%
	2-3 Week	1070	67.1%	93.9%	96.4%
	4-8 Week	1086	70.2%	93.6%	96.8%
	4-6 Month	996	74.8%	95.5%	98.6%
	7-11 Month	878	76.7%	94.5%	98.4%
	1 Year	840	73.6%	95.0%	98.6%
	2 Year	604	72.0%	94.0%	98.7%
	3 Year	376	69.9%	94.7%	98.4%
>-5 to -7 Diopters	1 Year	27	77.8%	100.0%	100.0%
	2 Year	14	85.7%	100.0%	100.0%
	3 Year	18	55.6%	100.0%	100.0%
>-7 to -10 Diopters	1 Year	161	73.3%	93.8%	99.4%
	2 Year	109	68.8%	94.5%	100.0%
	3 Year	69	73.9%	94.2%	100.0%
>-10 to -15 Diopters	1 Year	543	76.1%	95.6%	98.5%
	2 Year	388	74.2%	95.1%	98.5%
	3 Year	235	69.8%	94.0%	97.9%
>-15 Diopters	1 Year	109	60.6%	92.7%	97.2%
	2 Year	93	64.5%	88.2%	97.8%
	3 Year	54	70.4%	96.3%	98.1%

The following table shows the UCVA by lens power for all eyes implanted that were targeted for emmetropia.

Lens Group	Plano to:	N	20/20 or Better	20/40 or Better
All Diopter Powers	1-6 Day	720	13.1%	54.4%
	2-3 Week	686	18.8%	70.3%
	4-8 Week	687	26.5%	81.5%
	4-6 Month	623	35.0%	89.7%
	7-11 Month	556	39.6%	90.6%
	1 Year	521	39.9%	92.3%
	2 Year	379	36.9%	90.8%
>-5 to -7 Diopters	1 Year	11	45.5%	100.0%
	2 Year	7	0.0%	85.7%
	3 Year	8	0.0%	75.0%
>-7 to -10 Diopters	1 Year	90	51.1%	93.3%
	2 Year	60	50.0%	98.3%
	3 Year	32	50.0%	96.9%
>-10 to -15 Diopters	1 Year	347	38.9%	93.1%
	2 Year	252	36.9%	89.7%
	3 Year	148	36.5%	85.8%
>-15 Diopters	1 Year	73	30.1%	86.3%
	2 Year	60	28.3%	88.3%
	3 Year	37	27.0%	91.9%

### Directions For Use

1. Check the label on the lens package for proper lens model, dioptric power, and expiration date.
2. Inspect the blister pack. Ensure that it is not damaged.
3. Tap lightly on the lid before opening the lens container.
4. While keeping the container in a horizontal position, unscrew the cap and lift it.

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5. Grasp the lens gently with forceps.
6. Examine the lens carefully under the microscope for damage or particulate matter.
7. Rinsing the IOL with sterile balanced salt solution will remove the electrostatic charge.

**NOTE:** The IOL can become electrostatically charged and may stick to the lid of the lens container. The lens should be carefully examined to ensure that particles have not been attracted to it.

### Calculation of Lens Power

The physician should determine preoperatively the power of the lens to be implanted.

Lens power calculation methods are described in the following reference:

- van der Heijde, G.L., Some optical aspects of implantation of an IOL in a myopic eye, *European Journal of Implant Refractive Surgery*, Vol 1, Dec 1989, pgs 245-248

Physicians requiring additional information on lens power calculation should contact OPHTEC.

### Patient Registration Instructions and Reporting Registration

Each patient who receives an ARTISAN® Phakic IOL must be registered with OPHTEC at the time of lens implantation. Registration is accomplished by completing the Implant Registration Card that is enclosed in the lens package and mailing it to OPHTEC. Patient registration is essential for OPHTEC's long-term patient follow-up program and will assist OPHTEC in responding to Adverse Reaction Reports and/or potentially sight-threatening complications.

An Implant Identification Card is supplied in the lens package. This card should be given to the patient with instructions to keep it as a permanent record of the implant and to show the card to any eye care practitioner seen in the future.

### Reporting

Adverse Reactions and/or potentially sight-threatening complications that may reasonably be regarded as lens related and that were not previously expected in nature, severity or degree of incidence should be reported to OPHTEC immediately but no later than 10 days after occurrence. This information is being requested from all surgeons in order to document potential long-term effects of intraocular lens implantation, especially in younger patients.

Physicians must report these events in order to aid in identifying emerging or potential problems with ARTISAN® Phakic IOLs. These problems may be related to a specific lot of lenses or may be indicative of long-term problems associated with these lenses or with IOLs in general.

Physicians should use the following number when reporting adverse reactions or potentially sight

threatening complications involving OPHTEC intraocular lenses. **National: (561) 989-8767.**

### How Supplied

The IOL is supplied sterile and dry in a lens container, which is sealed in a blister pack and placed in a box together with the identifying labels.

### Expiration Date

Sterility is guaranteed unless the sterile pouch is damaged or opened. In addition, there is a sterility expiration date that is clearly indicated on the outside of the shelf-pack. The lens should not be used after the indicated date.

### Returned Lens Policy

The lens may be returned to the manufacturer for credit within 30 days of purchase. After 30 days it can be replaced or exchanged at no charge if not opened or damaged.

### DISTRIBUTED BY:

OPHTEC USA, Inc.  
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(561) 989-8767

### MANUFACTURED BY:

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