VALEANT

1400 North Goodman Street Rochester, NY 14609, USA

DESCRIPTION: Boston VST Ins / US / WILM

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SPECIAL INSTRUCTIONS: LENS0202.tif, LENS0203.eps

PRINT SUPPLIERS: Please refer to Valeant's *Print Supplier Guidelines*

BLACK	CYAN	YELLOW	MAGENTA				

PACKAGE INSERT

Boston® Orthokeratology (oprifocon A) Shaping Lenses

FOR OVERNIGHT WEAR FOR

BAUSCH+LOMB

Vision Shaping Treatment VST®

B+L

IMPORTANT

Please read carefully and keep this information for future use

This package insert is intended for the eye care practitioner, but should be made available to patients upon request. The eye care practitioner should provide the patient with the patient instructions that pertain to the patient's prescribed lens.

CAUTION: Federal law restricts this device to sale by, or on the order of a licensed practitioner.

Boston Orthokeratology (oprifocon A) Shaping Lenses should be fitted only by a contact lens fitter trained and certified in the fitting of conventional (non-reverse geometry) and reverse geometry contact lenses.

Nonsterile. Clean and condition lenses prior to use.

DESCRIPTION

Boston Orthokeratology (oprifocon A) Shaping Lenses are lathe cut contact lenses with spherical posterior surfaces in blue, green, red and yellow tinted versions. The posterior curve is selected to properly fit an individual eye for orthokeratology and the anterior curve is selected to provide the necessary optical power for a temporary reduction of myopia. A peripheral curve system on the posterior surface allows tear exchange between the lens and the cornea.

Boston Orthokeratology (oprifocon A) Shaping lenses are made from Boston® Equalens®II (oprifocon A) polymer with a water content of less than 1 percent. The material is available with or without an ultraviolet absorber, Uvinul D-49. The blue tinted lenses contain D&C Green #6 as a color additive. The green tinted lenses contain D&C Green #6 and D&C Solvent Yellow #18. The red tinted lenses contain D&C Red #17 as a color additive. The yellow tinted lenses contain C.I. Solvent Yellow #18 as a color additive.

LENS PARAMETERS AVAILABLE

Chord Diameter	9.0mm to 11.6mm
Center Thickness For low minus lens For plus lenses	0.20mm to 0.32mm 0.20mm to 0.32mm
Base Curve	7.30mm to 10.15mm
Reverse Curve	5.0 to 9.0 mm. Steeper than the base curve in proportion to the amount of correction
Alignment Curve 1	7.0 to 9.0 mm. Steeper than the base curve but flatter than the Reverse curve. Generally what to the Flat K of the cornea being fit
Alignment Curve 2	7.25 to 9.25 mm. Steeper than the base curve but flatter than AC1 and Reverse curve
Peripheral Curves	9.00mm to 15.00mm
Back Vertex Power	+1.50 to -5.00 Diopters

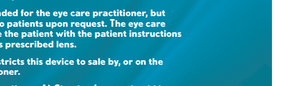

Figure 1: Representation of the reverse geometry lens design.

PHYSICAL PROPERTIES

The physical properties of oprifocon A

Refractive index	1.423
Light Absorbance (absorbance units/inch)	
Blue (640nm)	10.0
Green (640nm)	4.8
Yellow (420nm)	10.3
Red (525nm)	2.5
Wetting Angle	30 degrees by Captive Bubble
Specific Gravity	1.24
Hardness	114 Rockwell
Water Content	less than 1%
Oxygen Permeability	127* (85**)

* Gas to Gas Method
(x 10^{-11} (cm^2/sec) [mL O_2 x mm Hg]) @ 35°C)
** Polarographic Method (ISO/Fatt)

ACTIONS

The Boston Orthokeratology (oprifocon A) Shaping Lens produces a temporary reduction of myopia by changing the shape (flattening) of the cornea, which is elastic in nature. Flattening the cornea reduces the focusing power of the eye, and if the amount of corneal flattening is properly controlled, it is possible to bring the eye into correct focus and completely compensate for myopia.

The posterior surface of regular contact lenses generally aligns with the central cornea and rests directly on the corneal tear layer. Regular contact lenses are designed to cause little or no effect on the cornea but Boston Orthokeratology (oprifocon A) Shaping lenses are designed to purposely flatten the shape of the cornea by applying slight pressure to the center of the cornea when the patient is asleep.

After the lens is removed, the cornea retains its altered shape for all or most of one's waking hours. The lenses are designed to be worn overnight with removal during the following day. The Boston Orthokeratology (oprifocon A) Shaping Lenses must be worn at night on a regular schedule to maintain the orthokeratology effect, or the myopia will revert to the pretreatment level.

INDICATIONS

Boston Orthokeratology (oprifocon A) Shaping Lenses for Overnight Wear are indicated for use in the reduction of myopic refractive error in non-diseased eyes. The lenses are indicated for overnight wear as part of the Bausch + Lomb Vision Shaping Treatment VST® process for the temporary reduction of myopia up to 5.00 diopters with eyes having astigmatism up to 1.50 diopters. The lenses may only be disinfected using a chemical disinfection system.

Note: To maintain the Orthokeratology effect of myopia reduction, overnight lens wear must be continued on a prescribed schedule. Failure to do so can affect daily activities (e.g., night driving), visual fluctuations and changes in intended correction.

CONTRAINDICATIONS (REASONS NOT TO USE)

DO NOT USE the Boston Orthokeratology (oprifocon A) Shaping Lenses when any of the following conditions exist:

- Acute and sub-acute inflammations or infection of the anterior chamber of the eye.
- Any eye disease, injury, or abnormality that affects the cornea, conjunctiva or eyelids.
- Severe insufficiency of tears (dry eyes).
- Corneal hypoesthesia (reduced corneal sensitivity).
- Any systemic disease which may affect the eye or be exacerbated by wearing contact lenses.
- Allergic reactions of ocular surfaces or adnexa which may be induced or exaggerated by wearing contact lenses or use of contact lens solutions.
- Allergy to any ingredient, such as mercury or thimerosal, in a solution which is to be used to care for your Boston Orthokeratology (oprifocon A) Shaping Lenses.
- Any active corneal infection (bacterial, fungal or viral).
- If eyes become red or irritated.

WARNINGS

The practitioner should provide this warning to the patient.

PROBLEMS WITH CONTACT LENSES AND LENS CARE PRODUCTS COULD RESULT IN SERIOUS INJURY TO THE EYE.

It is essential that the patient follows the directions of the eye care practitioner and all labeling instructions for proper use of contact lenses and lens care products.

EYE PROBLEMS, INCLUDING CORNEAL ULCERS, CAN DEVELOP RAPIDLY AND LEAD TO LOSS OF VISION; IF THE PATIENT EXPERIENCES:

- **Eye Discomfort,**
- **Excessive Tearing,**
- **Vision Changes,**
- **Loss of Vision,**
- **Redness Of The Eye,**
- **Or Other Problems with their Eyes,**

THEY SHOULD BE INSTRUCTED TO IMMEDIATELY REMOVE THE LENSES, AND PROMPTLY CONTACT THEIR EYE CARE PRACTITIONER.

The risk of ulcerative keratitis has been shown to be greater among wearers of extended wear lenses than among wearers of daily wear lenses. The risk among extended wear lens wearers increases with the number of consecutive days that lenses are worn between removals, beginning with the first overnight use. This risk can be reduced by carefully following directions for routine lens care, including cleaning the storage case. Additionally, smoking increases the risk of ulcerative keratitis for contact lens wearers. It is recommended that contact lens wearers see their eye care practitioners twice each year or, if directed, more frequently.

Boston Orthokeratology (oprifocon A)Shaping Lenses are to be worn overnight with removal during all or part of each following day. Wearing the lenses continuously (extended wear) presents increased risk, which increases with the number of consecutive days that the lenses are worn between removals. Although the Bausch + Lomb Vision Shaping Treatment VST® process prescribes only overnight wear with removal during waking hours, and although the safety risks of overnight wear with removal upon wakening may not be as great as with extended wear, there is still increased risk beginning with the first overnight period.

PRECAUTIONS

Eye Care Practitioner

Clinical studies have demonstrated that Boston Orthokeratology (oprifocon A) Shaping Lenses are safe and effective for their intended use. However, the clinical studies may not have included all design configurations or lens parameters that are presently available in the material. Consequently, when selecting an appropriate lens design and parameters, the eye care practitioner should consider all factors that affect lens performance and the patient's ocular health; including oxygen permeability, wettability, central and peripheral thickness, and optic zone diameter.

The safety and effectiveness of the Boston Orthokeratology (oprifocon A) Shaping Lenses **have not** been clinically studied in adolescent and pediatric subjects.

The potential impact of these factors on the patient's ocular health should be weighed against the patient's need for refractive reduction; therefore, the continuing ocular health of the patient, and lens performance on the eye should be carefully monitored by the prescribing eye care practitioner.

Boston Orthokeratology (oprifocon A) Shaping Lenses are supplied non-sterile in an individual plastic case. The lens is shipped dry and must be cleaned and conditioned prior to use.

Patient

Patients should be informed of the following precautions

Solution Precautions

- Care of the Boston Orthokeratology (oprifocon A) Shaping Lenses may be accomplished with the use of either a two-bottle care regimen (separate conditioning solution and a separate cleaning solution) or a one-bottle care regimen (a multi action solution that is an all-in-one-solution). The use of a water rinse is limited to rinsing off the cleaning solution for a two-bottle care regimen (see package insert for instructions) but a water rinse should not be used with a one-bottle care regimen.
- Different solutions cannot always be used together, and not all solutions are safe for use with all lenses. Use only recommended solutions with the shaping lenses.
- Do not heat the wetting/soaking solution and lenses.
- Always use fresh unexpired lens care solutions.
- Always follow directions in the package inserts of the contact lens solutions used.
- Use only a chemical lens care system. Use of a heat (thermal) lens care system can cause damage by warping Boston Orthokeratology (oprifocon A) Shaping Lenses.
- Sterile unpreserved solutions, when used, should be discarded after the time specified in the labeling directions.
- Do not use saliva or anything other than the recommended solutions for lubricating or wetting lenses.
- Always keep the lenses completely immersed in the recommended storage solution when the lenses are not being worn (stored).

Handling Precautions

- Always wash and rinse hands before handling lenses. Do not get cosmetics, lotions, soaps, creams, deodorants, or sprays in the eyes or on the lenses. It is best to put on lenses before putting on makeup. Water-base cosmetics are less likely to damage lenses than oil-base products.
- Be certain that your fingers or hands are free of foreign material before touching your contact lenses. Microscopic scratches of the lenses may occur, causing distorted vision and/or injury to the eye.
- Carefully follow the handling, insertion, removal, cleaning, disinfecting, storing and wearing instructions in this booklet and those prescribed by your eyecare practitioner.
- Always handle your lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove lenses from the lens container unless specifically indicated for that use. Pour your lens into your hand.
- Do not touch the lens with your fingernails.
- To minimize lens warpage during cleaning, the lenses should be cleaned in the palm of the hand rather than between the thumb and fingers.

Lens Wearing Precautions

- CAUTION: Nonsterile. Clean and condition lenses prior to use.
- If the lens sticks (stops moving) on the eye, follow the recommended directions on Care for a Sticking Lens in the "Instructions for Wearers" booklet. The lens should move freely on the eye for the continued health of the eye. If non-movement of the lens continues, you should immediately consult your eye care practitioner.
- Never wear your contact lenses beyond the period recommended by your eye care practitioner.
- Avoid, if possible, all harmful or irritating vapors and fumes when wearing lenses.
- If aerosol products such as sprays are used while wearing lenses, exercise caution and keep eyes closed until the spray has settled.

Lens Case Precautions

- Contact lens cases can be a source of bacterial growth. To prevent contamination and to help avoid serious eye injury, always empty and rinse the lens case with fresh, sterile rinsing solution and allow to air dry.
- Lens case should be replaced monthly.

Discuss these topics with each patient:

- Wear of contact lenses during sporting activities
- Use of any medication in your eye
- Importance of adhering to the recommended follow-up schedule to assure the continuing health of your eyes.
- Informing your doctor (health care practitioner) about being a contact lens wearer
- Informing your employer of being a contact lens wearer. Some jobs may require the use of eye protection equipment or may require that contact lenses not be worn during work hours.
- What should be done if vision is inadequate during the day.

ADVERSE EFFECTS (PROBLEMS AND WHAT TO DO)

Patients should be informed that the following problems might occur:

- Eyes stinging, burning, itching (irritation), or other eye injury.
- Comfort is less than when lens was first placed on eye.
- Feeling of something in the eye, such as a foreign body or scratched area.
- Excessive watering (tearing) of the eyes
- Unusual eye secretions
- Redness of the eyes
- Reduced sharpness of vision (poor visual acuity)
- Blurred vision, rainbows, or halos around objects
- Sensitivity to light (photophobia)
- Dry eyes

Please refer to the Clinical Study Section of this package insert for adverse effects observed during the study.

If the patient notices any of these conditions, the patient should be instructed to **IMMEDIATELY REMOVE THE LENSES.**

The patient should be advised to follow these instructions:

- If the discomfort or problem stops, then look closely at the lens.
- If the lens is in any way damaged, DO NOT put the lens back on the eye. Place the lens in the storage case and contact the eye care practitioner.
- If the lens has dirt, an eyelash, or other foreign objects on it, or the problem stops and the lens appears undamaged, thoroughly clean, rinse and disinfect the lens; then reinsert it. Do not use a tap water rinse, use the approved conditioning solution as a rinsing agent.
- If the problem continues, IMMEDIATELY remove the contact lenses and consult the eye care practitioner.

When any of the above problems occur, a serious condition such as infection, corneal ulcer, neovascularization, iritis, persistent stromal edema or GPC (giant papillary conjunctivitis) may be present. The patient should be instructed to keep the lens off the eye and seek immediate professional identification of the problem and prompt treatment to avoid serious eye damage including corneal scarring, opacification, blindness or loss of eye.

CLINICAL STUDY DATA

Demographic Information

A total of 378 eyes (191 patients) were enrolled in the clinical study with 264 eyes (134 patients) completing a minimum of 9 months of contact lens wear. Data on 210 eyes (eyes with more complete effectiveness data) were analyzed for safety and effectiveness after 9 months of wear (the "core" group). In addition to this core group, 54 eyes were analyzed for safety data (the "adjunct" group). The entire population consisted of 128 females and 63 males, ranging in age from 17 to 64.

Effectiveness Outcomes

The average amount of myopia that can be expected to be corrected is shown in the following table. These values are only averages and some patients can be expected to achieve more or less than these averages.

Average Reduction in Myopia (Diopters) (210 Core Eyes)

Initial Myopia	Mean Reduction (D)	Mean Residual (D)
0 to -1.00	1.15	0.21
> -1.00 to -2.00	1.52	-0.15
> -2.00 to -3.00	2.39	-0.13
> -3.00 to -4.00	3.29	-0.22
> -4.00 to -5.00	3.85	-0.57
> -5.00 to -6.00	4.67	-0.68
> -6.00	4.88	-1.25

Uncorrected Visual Acuity (UCVA)

The primary efficacy endpoint for the core group was the number of eyes achieving at least 2 lines of improvement in uncorrected visual acuity with **at least 20/40 vision.** For the 210 Core eyes available at 9 months, 199 eyes (95%) met these criteria of success, while 11 eyes did not achieve this successful outcome.

PRIMARY EFFICACY ENDPOINT AT 9 MONTHS STRATIFIED BY PRE-TREATMENT MYOPIA CORE EYES (210)

PRETREATMENT MYOPIA (MRSE)									
	Orig -0.000*	>.000 to -2.000	>-2.000 to -3.000	>-3.000 to -4.000	>-4.000 to -5.000	>-5.000 to -6.000	>-6.000 to -7.000	Total
	n	n	n	n	n	n	n	n
A. Eyes at 9 months with 2 lines improvement and 20/40 or better	5	60	72	34	22	5	1	199
B. Eyes at 9 months not meeting above criteria, data available	1	3	4	0	3	0	0	11
C. Eyes enrolled and available at 9 months	6	63	76	34	25	5	1	210
Percent who met "success" criteria (A/C)x100	833	952	947	1000	880	1000	1000	948
MRSE Mean	021	-.015	-.013	-.022	-.057	-.068	-.125	
Std Dev	097	-.064	-.050	-.051	-.114	-.068	-.00	

* only 1 eye had an MRSE =.100 (.063)

Post-treatment visual acuity was assessed on the 210 analyzed core eyes. Seventy-three percent achieved 20/20 or better, 95% achieved 20/40 or better.

Accuracy

At 9-months, 80 percent of the core eyes achieved a reduction of myopia to within 0.50 D of target and 93% achieved a reduction to within 1.00 D of target. The accuracy of the temporary reduction in myopia is given in the following table, which also shows the final acuity without lenses. However, accuracy of correction is less with correction higher than 4.00D than with those less than 4.00D.

VISUAL OUTCOME ACCURACY OF THE TEMPORARY REDUCTION OF MYOPIA, FINAL ACUITY WITHOUT CONTACT LENSES (Core Eyes at 9-Months)

*Initial Myopia***	*% Within 0.50D of Target**	*%Within 1.00D of Target**	*% With Final VA 20/20 or better**	*% With Final VA 20/40 or better**
+0 to -1.00D	100%	100%	100%	100%
-1.25 to -2.00D	81%	93%	82%	94%
-2.25 to -3.00D	87%	96%	77%	94%
-3.25 to -4.00D	79%	94%	71%	100%
-4.25 to -5.00D	60%	88%	64%	95%

* 100=# reported/# in category
** Manifest Refraction Spherical Equivalent

Wearing Time

The lenses were intended for overnight wear only. The average wear time was reported to be between 8 and 10 hours per night, and there was no apparent relationship between the number of hours of wear and the visual outcome, for any amount of pretreatment myopia.

Effects on Astigmatism

Either increases or decreases in astigmatism may occur following orthokeratology. Of the 210 analyzed eyes, 35% showed no change in refractive astigmatism, 41% showed a decrease of one diopter or less, 2% showed a decrease greater than one diopter, 20% showed an increase of one diopter or less, and 2% showed an increase greater than one diopter.

OVERNIGHT WEAR SAFETY SUMMARY

In this study all eyes were evaluated for safety of overnight wear for orthokeratology to treat myopia and myopia with astigmatism. Two hundred and sixty-four eyes were followed for 9 months. The data on best corrected acuity, adverse events, slit lamp findings and symptoms provide reliable indications of the safety of oprifocon A in this treatment modality.

Best Spectacle Corrected Visual Acuity (BSCVA)

The majority of core eyes (those eyes with more complete effectiveness data upon which the primary effectiveness determinations can be made), 73% had no change in BSCVA from baseline. 18 % had a gain of 1 line, <1% had a gain of 2 lines, and 1 % had a gain of >2 lines in BSCVA as compared to baseline. Concurrently, 8% had a loss of >1 line as compared to baseline. No core eyes had a loss of ≥2lines of BSCVA.

For the 54 completed adjunct eyes (those subjects for which incomplete data was collected but enough data is provided to use as safety data) the change in lines of BSCVA at the 9-month post-treatment interval showed 41% had no change in BSCVA from baseline, and 1% gained 1 line. There were 4% with loss of 1 line in BSCVA. Data were not reported for 29 eyes.

When considering all eyes entered into the study, there were a total of 42 incidents (in 34 eyes) of at least a temporary reduction of ≥ 2 lines of BSCVA during the course of the study.

Only 12 of the 42 incidents occurred after 3 months. Duration of the vision loss was not accurately determined in all cases, but for incidents in which there is some documentation and recovery was demonstrated, length of time to documented recovery varied from 1 day to 9 months. Thirty-three eyes had a duration of reduced vision of > 7 days.

Four eyes in 3 patients showed a reduction of ≥ 2 lines of best corrected acuity from initial visit to last study visit. One of these eyes was subsequently documented to return to normal acuity. No significant ocular abnormalities were observed in these eyes with biomicroscopy at the time of study exit.

Slit Lamp Findings

For 2,907 eye exams, there were 14 exams showing slit lamp findings greater than grade 2 reported as follows: grade 3 for staining (3 incidents); grade 4 for staining (2 incidents); grade 3 for injection (2 incident); grade 3 "other" (4 incidents); and ungraded (3 incidents: 2 staining and 1 tarsal abnormality). All findings greater than grade 2 resolved without further complications. There were 5 slit lamp findings > Grade 2 or ungraded at the 1-Day Visit, all in the adjunct. The most significant of the > Grade 2 findings, were 3 Grade 3 Corneal Staining cases, 2 Grade 4 Corneal Staining cases, 1 case of Corneal Infiltrates (grade 3) and 2 Cases (2 eyes of 1 subject) of trace Iritis.

Symptoms, Problems and Complaints

Subjects were asked to report symptoms and complaints at each follow-up visit. For core and completed adjunct eyes, poor distance vision was reported for 17% (369/2389), flare or ghosting were reported for 9% (216/2389), and all other symptoms (poor near vision, red eye, excessive lens awareness/pain, excessive discharge, burning/itching, and photophobia) were reported for 8% (188/2389) throughout the study. It appears that the eyes with initial myopia above 3.00D had a higher incidence of these visual disturbances.

Discontinuations

Of the 90 adjunct subjects, 55 subjects (110 eyes) discontinued before completing 9 months of wear, for reasons as listed in the following table.

REASONS FOR DISCONTINUATION		
Clinical Reason*	**# eyes**	**% of all eyes**
Unacceptable vision	52	14%
Lack of Comfort	28	8%
Unacceptable physiology	12	3%
Non-clinical Reason		
Lost-to-follow-up	38	10%
Other**	10	3%

* Several subjects reported more than 1 reason for discontinuation, without giving any priority to the reasons.

** "Other" included returned to spectacles (2 eyes), night vision bothered (2 eyes), wanted prior uncorrected near vision (2 eyes), financial (2 eyes), and could not maintain visit schedule (2 eyes).

Adverse Events and Complications

There were 12 significant lens-related adverse events reported in10 subjects. Two eyes had bilateral grade 4 staining with significant decrease in vision to 20/80. One eye had grade 3 corneal staining secondary to a dislodged lens. One eye had significant corneal distortion with reduced vision to 20/200 and rippling on the cornea. Two eyes had bilateral iritis with trace cells and flare in both eyes. One eye had corneal infiltrates.

Two eyes had abrasion (grade 3 staining). One eye had reduction of BSCVA to 20/50 secondary to a decentered lens. One eye had reduction of BSCVA to 20/60 due to central staining. One eye had reduction of BSCVA to 20/60 with no reason given.

All of these eyes that showed acuity reductions were documented as returning to normal vision, except two eyes of one subject with severe corneal staining that showed ≥2 lines loss of BSCVA. The return to pretreatment VA was not recorded in the case report form of this subject although the subject returned to soft contact lens wear and verbally reported that vision was normal. Of the 10 subjects for which adverse events were reported, 4 subjects discontinued the study. All adverse events resolved without further complications.

Change in Corneal Cylinder

The reduction in refractive error and improvement in unaided visual acuity is the result in part of a change in the corneal radius as measured by keratometry. The keratometer measures the corneal curvature in the two principal meridians at a chord diameter slightly less than 3 millimeters. The keratometer does not provide data of the local curvature inside or outside of the location of its measurement.

14% of all treated eyes manifested more than one diopter of increase in corneal cylinder from baseline to the nine month visit. The core group contained 26 eyes with greater than 1 D increase and the adjunct group contained of 24 eyes with greater than 1 D increase.

There were 7 eyes in the core group and 11 in the adjunct group that had increases (initial to patient's last visit) in corneal cylinder of >2 D. No eye with cylinder increase >1 D had a BSCVA at exit worse than 20/30.

Summary of Key Safety Variables

A summary of key safety variables is presented in the following table

SUMMARY OF KEY SAFETY VARIABLES		
Criteria	**All Treated Eyes (364)**	
	n	**%**
Significant Adverse Events	12*	3
Loss of ≥ 2 lines BSCVA† ‡	4	1
BSCVA worse than 20/40†	1	<1
Increase of >1 D Refractive Cylinder†	12	3
Increase of >1 D Corneal Cylinder†	50	14

* Includes 4 discontinued subjects (6 eyes).

† From baseline to exit visit

‡ there were 42 incidents (in 34 eyes) of at least a temporary reduction of ≥ 2 lines of BSCVA during the course of the study. All except 4 discontinued eyes were documented as returning to normal during the study; one eye was documented to return to normal acuity after the study. No significant ocular abnormalities were observed in these eyes with biomicroscopy at the time of study exit.

POST LENS REMOVAL (REGRESSION STUDY) UNCORRECTED VISUAL ACUITY (UCVA)

The effects of wearing your lenses at night are not permanent and slowly diminish after you remove your lenses. While this does not present a problem for most wearers, it is important to realize for some patients their vision at the end of the day may not be fully satisfactory for highly demanding visual tasks. Although this may not be an issue for most wearers, the eye care practitioner should consider each patient's "late in the day" circumstance to discuss what steps the patient should take if this is a concern. The objective of this study was to evaluate the post-lens removal regression in subjects who had achieved refractive stability" following overnight orthokeratology treatment using Boston Orthokeratology (oprifocon A) Shaping Lenses.

Regression of Visual Acuity

To help you assess the change in vision over time following lens removal, subjects that achieved refractive stability in this clinical study were evaluated at 5-Hour, 24-Hour, 3-Day, and 1-Week Visits after removing their lenses. One hundred eighty four eyes (105 subjects) achieved refractive stability" and completed the Regression Phase.

The following table presents a summary of uncorrected distance visual acuity (UCVA) through the Regression Phase. At the beginning of the regression phase, 100% of the eyes that achieved refractive stability had UCVA of 20/40 or better**. At the 5-Hour visit of the Regression Phase, 98.9% of the eyes had 20/40 or better. By the 24-Hour visit, 66.5% of the eyes still had UCVA of 20/40 or better.

Summary of uncorrected distance visual acuity (UCVA) through the Regression Phase

	At Lens Removal		5-Hour Visit		24-Hour Visit		3-Day Visit		1-Week Visit	
	#	%	#	%	#	%	#	%	#	%
20/15	8	4.3	10	5.4	4	2.2	0	0	0	0
20/20	136	73.9	131	71.2	48	26.4	20	11.3	3	1.7
20/25	26	14.1	22	12.0	25	13.7	14	7.9	7	3.9
20/30	10	5.4	16	8.7	21	11.5	23	13.0	8	4.4
20/40	4	2.2	3	1.6	23	12.6	20	11.3	20	11.0
Worse than 20/40	0	0	2	1.1	61	33.5	100	56.5	143	79.0
Total	184	100.0	184	100.0	182	100.0	177	100.0	181	100.0

* Refractive stability was considered to be achieve when on two visits, separated by a minimum of 27 days in the same lens, the refraction (defined as the MRSE) varied not more than + 0.50D.

** Most states require 20/40 in better eye for an unrestricted driver's license.

At the start of the Regression Phase, there were 101 (54.9%) eyes that had a Manifest Refractive Spherical Equivalent (MRSE) between ± 0.25D and 134 (72.8%) between ± 0.50D. For these eyes, the mean time (in hours) following lens removal until MRSE regression to –1.00D or worse is summarized in the following table for completed eyes achieving stability. The eyes with greater pretreatment myopia had less time (in hours) until MRSE regression to –1.00D. Similarly, there was a tendency for the eyes with greater pretreatment myopia to have less time until they regressed to 20/40 or worse as time progressed.

Average number of hours until Manifest Refractive Spherical Equivalent (MRSE) regressed to –1.00D following lens removal

	Pretreatment Myopia (MRSE)				
Refraction (MRSE at Lens Removal	-1.00D to -2.00D	-2.12 to -3.00D	-3.12 to -4.00D	-4.12 to -5.00D	-5.12 to -5.75D
+0.37 to +0.50D	156.3	62.2	32.0	-	-
+0.12 to +0.25D	136.9	56.2	28.7	24.0	-
Plano	92.0	63.3	25.2	58.0	-
-0.12 to -0.25D	101.8	56.1	28.5	29.0	25.0
-0.37 to -0.50D	75.7	24.7	44.6	7.0	5.0

POSTMARKET SURVEILLANCE STUDY INCIDENCE RATE OF MICROBIAL KERATITIS IN PEDIATRIC PATIENTS COMPARED TO ADULTS

The purpose of this postmarket surveillance study was to determine whether the incidence of microbial keratitis in pediatric patients, defined as persons under the age of 18, is higher than in adult patients wearing orthokeratology reshaping lenses overnight in patients fitted with either Paragon CRT®, Paragon CRT® 100, or Boston Orthokeratology (oprifocon A) Shaping Lenses. Bausch + Lomb and Paragon Vision Sciences collaboratively sponsored the study. The study question was whether the incidence of microbial keratitis was higher in pediatric patients than in adult patients.

STUDY DESIGN

The study identified patients fit by a randomly selected, stratified (low- and high-volume prescribers) sample of practitioners. The patient-sampling strategy was designed to identify enough patients that had been fit with corneal reshaping lenses with sufficient follow-up to provide 2000 patient-years of exposure. The primary endpoints for the study were defined as the incidence of microbial keratitis in pediatric and adult groups and the difference in rates between the two age groups.

Study Population

The retrospective study design did not employ patient enrollment but rather the selection of practitioners. The random sampling strategy recruited equal numbers of low- and high-volume practitioners, but limited the number of patients contributed by any one practitioner to 50, in order to minimize the respondent burden and to avoid any single practice contributing a substantial proportion of the sample.

Patients were not prospectively enrolled according to strict inclusion and exclusion criteria, but instead were identified retrospectively through lens orders from 2005 and 2006.

Safety Evaluation

Participating practitioners reviewed their medical records for up to 50 patients, selected at random. Only data on lens wear from 2005 onwards and cases of possible microbial keratitis from 2005 onwards were analyzed in order to minimize bias.

A total of 86 practitioners completed a standardized summary form to capture patient age, fitting date, and duration of lens wear. In addition, practitioners were asked to report any potential cases of microbial keratitis associated with the selected corneal reshaping lenses using the criterion of a painful red eye that required a visit to a doctor's office. The definition of microbial keratitis was one or more corneal stromal infiltrates greater than 1 mm in size, pain more than mild, and one or more of the following: anterior chamber reaction more than minimal, mucopurulent discharge, or positive corneal culture. Also considered was whether the practitioner prescribed treatment consistent with the standard of care for microbial keratitis in terms of choice of medication, frequency and duration of use.

An Outcomes Assessment Panel reviewed all potential cases of microbial keratitis masked to patient age. The Panel members were chosen based on their expertise in the assessment, evaluation, and management of contact lens related complications. Individuals with associations with either sponsor were excluded.

The incidence rate and confidence intervals were estimated as the ratio of the number of cases in an age group divided by the years of lens wear. Confidence intervals for the difference in the incidence rates between pediatric and adult patients were also calculated.

A conservative analysis of 685 patients who began wear of overnight corneal reshaping lenses after January 2005 and had at least one year of documented lens wear is presented in Table 2. These patients contribute a total of 1415 patient-years of lens wear (794 pediatric and 621 adult).

TABLE 2
Incidence of Microbial Keratitis Patients with at Least 1 Year of Lens Wear In 2005 and 2006

	Pediatric Patients	Adults	Overall
N	378	307	685
Cases	2	0	2
Years at Risk	794	621	1415
Incidence Rate per 10,000 patient-years	25.2	0.0	14.1

RESULTS

Of the 200 randomly selected practitioners, 9 could not be contacted. Of the 191 practitioners that could be contacted, 119 agreed to participate (62%) and of these, 86 returned completed forms, 11 withdrew, and 22 failed to submit data in spite of multiple reminders. Of the 72 non-participating practitioners (191 minus 119), approximately 10% declined to participate and the remainder would not return repeated phone calls from the Lead Investigator. The completed forms corresponded to 2,202 lens orders and represented unique 1494 patients. Limiting the sample to those beginning lens wear in 2005 or 2006 provided 2599 patient-years of lens wear (exceeding the goal of 2000) for 1317 patients (677 children and 640 adults). At the original fitting date the mean age of the pediatric group was 12.2 ± 2.5 years and the mean age of the adults was 38.0 ± 11.1 years. The mean follow-up for the pediatric group was 2.1 ± 0.8 years, with 620 (92%) having at least 12 months of follow-up. The mean follow-up for the adults was 1.8 ± 1.0 years, with 497 (78%) having at least 12 months of follow-up.

The Outcome Assessment Panel identified two cases of microbial keratitis within 2599 patient-years of overnight corneal reshaping lens wear. Both cases of microbial keratitis occurred at least one year after fitting and neither resulted in any documented long-term loss of best corrected visual acuity. Table 1 summarizes the incidence data for microbial keratitis based on the 2599 patient-years of lens wear. The overall estimated incidence of microbial keratitis is 7.7 per 10,000 patient-years including the estimated incidence of 13.9 per 10,000 patient-years for the pediatric group, and 0.0 per 10,000 patient-years for adults.

TABLE 1
Incidence of Microbial Keratitis Patients with at Least 3 Months of Lens Wear In 2005 and 2006

	Pediatric Patients	Adults	Overall
N	677	640	1317
Cases	2	0	2
Years at Risk	1435	1164	2599
Incidence Rate per 10,000 patient-years	13.9	0.0	7.7

* / Poggio EC, et al. The incidence of ulcerative keratitis among users of daily-wear and extended-wear soft contact lenses. N Engl J Med. 1989 Sep 21;321(12):779-83.

STUDY STRENGTHS

Previous published studies have reported individual or small series of patients presenting with microbial keratitis, none have compared incidence among adult and pediatric populations. This was a retrospective study which looked backward over a period of time to compare the groups. Retrospective studies are particularly useful in investigating diseases or adverse effects with low incidence of occurrence. This was a study (2599 patient-years) of randomly selected patients fitted by 86 randomly selected practitioners over two years. Cases were classified by an independent group of experts using clear and established criteria and without knowledge of whether the patient was a child or an adult.

STUDY LIMITATIONS

Retrospective studies are useful in providing estimates of relative risk; however, there can be limitations associated with a retrospective design involving adverse events occurring in the past. Bias can be introduced with a retrospective design, for example, by practitioners or patients declining to participate. While study sites were selected at random, participation was voluntary and practitioners who had observed cases of microbial keratitis may have been less willing to participate. Although the retrospective analysis was of patients fitted over a two-year period, the incidence rate calculations assume that the occurrence of microbial keratitis is constant over time, i.e. there are assumptions associated with the use of constant incidence denominators. Such assumptions may not be valid as the risk my change over time. Patients were selected at random but lens wear was not documented beyond practitioner report. The practitioners' inability to confirm whether some patients wore the study lenses and whether they wore the lenses for the minimal time required may have inflated the total years at risk, thus artificially depressing the reported incidence of microbial keratitis and increasing the statistical power of the study. Nonetheless, 1158 of the 1317 patients had at least one year of wear documented by the practitioner and 81 patients were documented as discontinued by the practitioner. A total of 78 patients can be regarded as lost to follow-up. Only 86 out of 200 (43%) targeted practitioners enrolled in the study by returning the completed form. The classification of microbial keratitis was determined by an Outcome Assessment Panel without direct contact with the patient or photographs. These factors should be considered when evaluating the significance of the results.

CONCLUSIONS

The primary goal of the study was to compare the risk of microbial keratitis between children and adults with at least 3 months of lens wear.

In this retrospective study, the following rates of microbial keratitis were observed:

- In Children: 2 cases of microbial keratitis were reported (13.9 per 10,000 patient-years). Both cases of microbial keratitis occurred at least one year after fitting and neither resulted in any documented long-term loss of best corrected visual acuity.
- In Adults: 0 cases of microbial keratitis were reported.

Results from this retrospective observational study are tentative and not conclusive. Results from a large, well-controlled prospective clinical trial can provide more definitive results.

Data on rates of infectious corneal ulcers in children wearing other types of contact lenses is not available. For comparison, Poggio et al. (1989),* estimated the risk to be ~21 per 10,000 patient-years for extended-wear soft contact lenses (lenses worn overnight) and ~4 per 10,000 patient-years for daily wear soft contact lenses.

FITTING

Caution: Boston Orthokeratology (oprifocon A) Shaping Lenses should be fitted only by a contact lens fitter trained and certified in the fitting of conventional (non-reverse geometry) and reverse geometry contact lenses.

Conventional methods of fitting rigid contact lenses for orthokeratology DO NOT APPLY to the Boston Orthokeratology (oprifocon A) Shaping Lens. For a description of fitting techniques, refer to the Fitting Guide for Boston Orthokeratology (oprifocon A) Shaping Lenses for Overnight Wear for Bausch & Lomb Vision Shaping Treatment VST; copies of the Fitting Guide are available from:

Bausch & Lomb Incorporated
1400 North Goodman Street
Rochester, New York 14609
1 (800) 333-4730

RECOMMENDED WEARING SCHEDULE

Although many practitioners have developed their own initial wearing schedules, the following sequence is recommended as a guideline. Patients should be cautioned to limit the wearing schedule as recommended by their eye care practitioner regardless of how comfortable the lenses feel.

Wearing Schedule: On night one lenses should be inserted at a time early enough to achieve 8 to 10 hours of closed eye wearing time (sleep). A well fit lens provides for centration with the eye closed. The effects of lid interaction on blinking and gravity may result in lens decentration during open eye wear. The patient should place the lens(s) in their eye 15 to 20 minutes before going to sleep.

Be aware "when in doubt, take it out". It is important that the new wearer not sleep in a lens that has a significant foreign body sensation. In the event of foreign body sensation, instruct the patient to remove the lens, clean and re-wet it; and again place the lens in the eye. If the sensation continues, remove the lens. The lens should not be worn.

Appointment Schedule: The patient should report for follow-up evaluation the morning after the first overnight wear. The visit is best scheduled within a few hours of awakening and the patient should report with lenses in place. This visit provides an excellent opportunity to evaluate lens centration and potential lens adherence.

Upon the absence of clinical signs and complications, the patient may be instructed to continue overnight wear of the lenses until the next scheduled follow-up visit.

An alternate daytime wear schedule may be offered at the practitioner's discretion.

Myopic Reduction Maintenance Lens (Retainer Lens) Schedule

After a period of several days, or when the eyecare practitioner is satisfied that the patient has adapted to the Boston Orthokeratology (oprifocon A) Shaping Lenses, the eyecare practitioner may optimize the wearing schedule for an individual patient to monitor the duration of visual improvement. This may continue as long as the patient can see clearly. When it is found that the patient experiences a visual decrement following lens removal, the schedule of overnight wear must be modulated to maintain visual performance.

LENS CARE DIRECTIONS

The lens care products listed below are recommended by Bausch & Lomb Incorporated for use with the Boston Orthokeratology (oprifocon A) Shaping lenses.

Chemical Lens Care System
Two Bottle System:
Boston ADVANCE® Cleaner or Boston® Cleaner
Boston ADVANCE® Comfort Formula
Conditioning (soaking) Solution or Boston®
Conditioning Solution

OR

One Bottle System:
Boston SIMPLUS® Multi-Action Solution (Removes Protein, Cleans, Disinfects, Conditions, Cushions).

The directions found in the package inserts from these products should be followed. Failure to adhere to these procedures may result in the development of serious ocular complications. A patient should not switch from one care system to another unless it has been determined by the eye care practitioner that this is necessary. Do not mix or alternate these chemical storage systems unless so indicated on the product label.

Inform the patient of the following lens care suggestions:

- Always wash and rinse your hands before handling your shaping lenses
- Never use tweezers or other tools to remove your lenses from the lens container. Pour the lens into your hand.
- Boston Orthokeratology (oprifocon A) Shaping Lenses must be both cleaned and disinfected each time you remove them. One procedure does not replace the other. Cleaning is necessary to remove mucus and film from the lens surface. Disinfecting is necessary to destroy harmful germs. To minimize lens warpage during cleaning, the lenses should be cleaned in the palm of the hand rather than between the thumb and fingers.
- Care of the Boston Orthokeratology (oprifocon A) Shaping Lenses may be accomplished with the use of either a two-bottle care regimen (separate conditioning solution and a separate cleaning solution) or a one-bottle care regimen (a multi action solution that is an all-in-one-solution). The use of a water rinse is limited to rinsing off the cleaning solution for a two-bottle care regimen (see package insert for instructions) but a water rinse should not be used with a one-bottle care regimen.

  For a two-bottle system – Clean one lens first. The recommended procedure is to always clean the same lens first to avoid mix-ups. Rinse the lens thoroughly with tap water to remove the cleaning solution. Place the lens into the correct storage chamber and fill the chamber with the recommended disinfecting solution as recommended by your eye care practitioner. Clean and rinse the other lens in the same manner and place it in its chamber with fresh disinfecting solution.

  For a one-bottle system – Clean one lens first. The recommended procedure is to always clean the same lens first to avoid mix-ups. Rinse the lens with the one-bottle solution DO NOT USE A TAP WATER RINSE when using a one-bottle system. Place the lens into the correct storage chamber and fill the chamber with the recommended one-bottle disinfecting solution as recommended by your eye care practitioner. Clean and rinse the other lens in the same manner and place it in its chamber with fresh one-bottle disinfecting solution.
- Tightly close the top of each chamber of the lens storage case.
- To disinfect your lenses, leave them in the solution for at least the period indicated on the product label.
- Leave the lenses in the closed storage case until you are ready to put the Boston Orthokeratology (oprifocon A) Shaping Lenses in your eyes. DO NOT RINSE THE LENSES WITH TAP WATER PRIOR TO PLACING THE LENSES IN YOUR EYES.

LENS CASE CLEANING AND MAINTENANCE

Contact lens cases can be a source of bacteria growth. Lens cases should be emptied, cleaned, rinsed with solutions recommended by the case manufacturer, and allowed to air dry. Lens cases should be replaced monthly.

ENZYME CLEANING

The eye care practitioner may recommend enzyme cleaning. Enzyme cleaning does not replace routine cleaning and disinfecting. The patient should carefully follow the instructions in the enzymatic cleaning labeling.

EMERGENCIES

If chemicals of any kind (household products, gardening solutions, laboratory chemicals, etc.) are splashed into the eyes, the patient should flush eyes immediately with tap water and then remove lenses promptly. The patient should CONTACT THE EYE CARE PRACTITIONER OR VISIT A HOSPITAL EMERGENCY ROOM WITHOUT DELAY.

HOW SUPPLIED

Each lens is supplied non-sterile in an individual plastic case. The case, packing slip or invoice is marked with the base curve, power in diopters, diameter, center thickness, color, and lot #.

REPORTING OF ADVERSE REACTIONS

All serious adverse experiences and adverse reactions observed in patients wearing or experienced with the lenses should be reported immediately to the manufacturer.

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