**PACKAGE INSERT**

# Paragon Z CRT®

Manufactured in
Menicon Z® (tisilfocon A)

## RIGID GAS PERMEABLE CONTACT LENSES FOR CONTACT LENS CORNEAL REFRACTIVE THERAPY

OVERNIGHT WEAR

**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.

CAUTIONS: Federal law (US) restricts this device to sale by, or on the order of a licensed practitioner.

Contact lenses for Corneal Refractive Therapy should be fitted only by a contact lens fitter trained and certified in the fitting of conventional and sigmoid geometry contact lenses.

Nonsterile. Clean and condition lenses prior to use.

**WARNING:** 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 YOU FOLLOW YOUR EYE CARE PRACTITIONER'S DIRECTIONS AND ALL LABELING INSTRUCTIONS FOR PROPER USE OF YOUR CONTACT LENSES AND LENS CARE PRODUCTS. EYE PROBLEMS, INCLUDING CORNEAL ULCERS, CAN DEVELOP RAPIDLY AND LEAD TO LOSS OF VISION; THEREFORE, IF YOU EXPERIENCE EYE DISCOMFORT, EXCESSIVE TEARING, VISION CHANGES, REDNESS OF THE EYE, OR OTHER PROBLEMS WITH YOUR EYES, IMMEDIATELY REMOVE YOUR LENSES, AND PROMPTLY CONTACT YOUR EYE CARE PRACTITIONER OR ATTENDING HOSPITAL EMERGENCY ROOM PHYSICIAN.**

# Paragon Z CRT®
# CONTACT LENSES FOR CORNEAL REFRACTIVE THERAPY OVERNIGHT WEAR

## DESCRIPTION

Paragon Z CRT® contact lenses are manufactured from Menicon Z® (tisilfocon A). The lenses are designed to have congruent anterior and posterior surfaces each consisting of three zones:

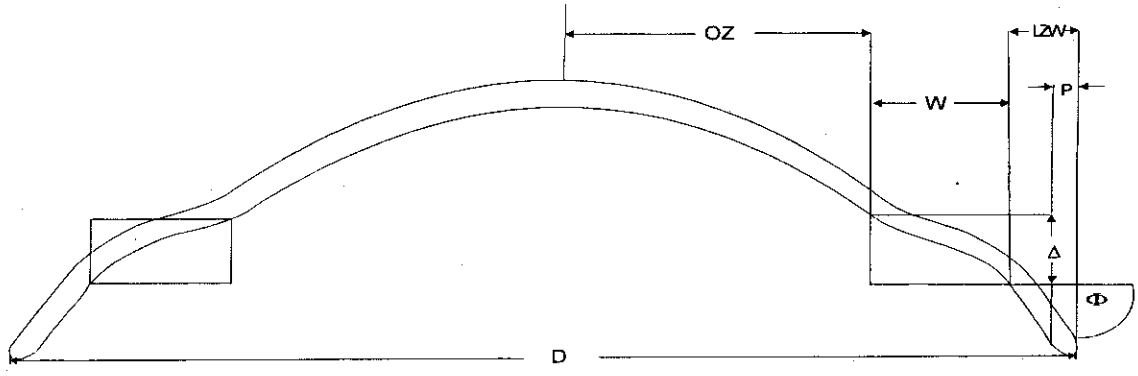
1. The central spherical zone.
2. A mathematically designed sigmoidal corneal proximity "Return Zone".
3. A non-curving "Landing Zone".

The lens design also includes a convex elliptical edge terminus smoothly joining the anterior and posterior surfaces.

Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy are to be worn overnight with removal during all or part of each following day. The lens material (tisilfocon A) is a thermoset copolymer derived from fluoro-methacrylate and siloxanylstyrene bound by crosslinking agents. The lenses for Corneal Refractive Therapy are available as lathe cut firm contact lenses with a light blue tint. The blue tinted lens contains D&C Green No. 6. A UV absorber (Benzotriazol) is added as an additive during the manufacturing process.

**LENS PARAMETERS AVAILABLE** (See drawing)

| | |
|---|---|
| Overall Diameter (D) | 9.5 to 12.0 mm |
| Central Base Curve Radius | 6.50 to 10.50 mm |
| Optical Zone Semi Chord (OZ) | 2.50 to 3.50 mm |
| Return Zone Width (w) | 0.75 to 1.5 mm |
| Return Zone Depth (Δ) | to 1.0 mm |
| Landing Zone Radius | to infinity |
| Landing Zone Angle (Φ) | -25° to -50° |
| Landing Zone Width (LZW) | 0.5 to 2.75 mm |
| Peripheral Edge Curve Width (P) | 0.04 mm to LZW |
| Dioptric Powers | -2.00 to +2.00 Diopters |



## ATTRIBUTES OF THE PARAGON Z CRT® LENS (tisilfocon A)

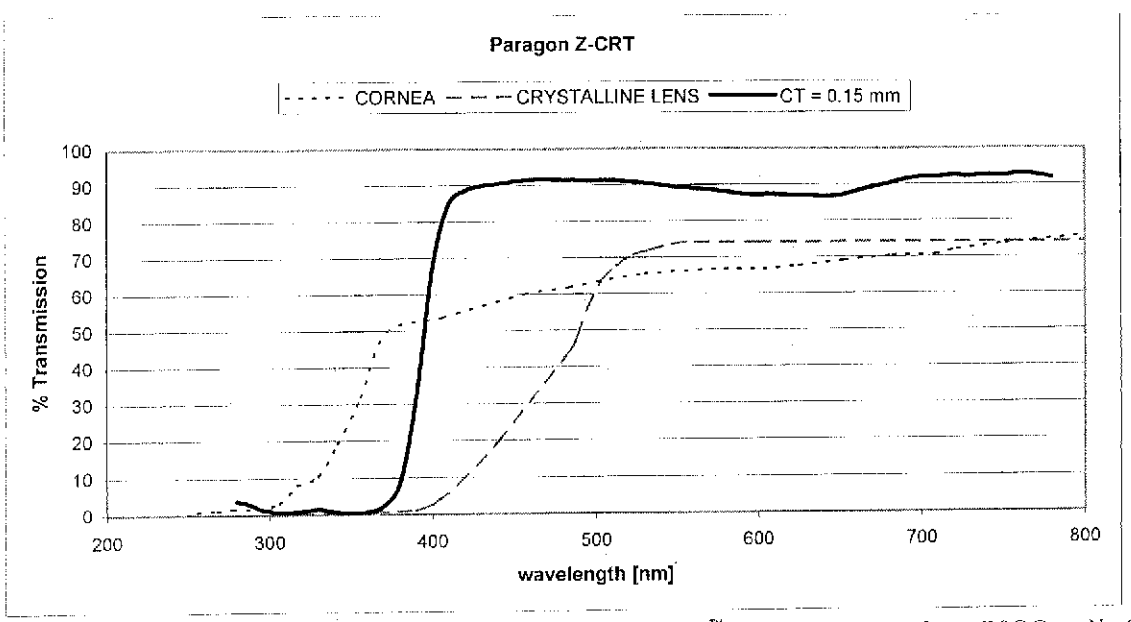
| | |
|---|---|
| Refractive Index | 1.436 (Nd at 25°C) |
| Light Transmittance | |
| Visible Region | >95% (380nm – 780nm) |
| Ultraviolet Region | <6% (210nm – 380nm) |
| (sample thickness 0.08mm) | |
| Wetting Angle (after soaking) | 24° |
| Specific Gravity | 1.20 |
| Water Absorption | <0.5% by weight |
| Oxygen Permeability[+] | 163 Dk x $10^{-11}$ |

[+] ($cm^2$/sec) (mL $O_2$)/ (mL x mm Hg) ISO/ANSI Method, ISO 9913-1

**OXYGEN PERMEABILITY - CRT® LENS DESIGN**

| Material | Power | Oxygen Permeability (Revised Fatt Method) Dk x $10^{-11}$ | Oxygen Permeability (ISO Method*) Dk x $10^{-11}$ | Center Thickness (mm) | Harmonic Mean Thickness** (mm) | Oxygen Transmissibility (ISO) Dk/l x$10^{-9}$ |
|---|---|---|---|---|---|---|
| Menicon Z | -2.00 | 145 | 163 | 0.145 | 0.163 | 99 |
| Menicon Z | Plano | 145 | 163 | 0.163 | 0.166 | 98 |
| Menicon Z | +2.00 | 145 | 163 | 0.180 | 0.168 | 98 |

* ($cm^2$/sec) (mL $O_2$)/ (mL x mm Hg) ISO/ANSI Method, ISO 9913-1
** Sammons, W.A., "Contact Lens Thickness and All That", The Optician, 12/05/80.




Menicon Z (tisilfocon A) Contact Lens - Spectral transmittance curve for Menicon Z™ (tisilfocon A ) Contact Lens - D&C Green No. 6 and UV absorbing agent (sample thickness Menicon Z™ (tisilfocon A) lens polymer plate = 0.08mm, representing the thinnest marketed version of the lens).
CORNEA - Human cornea from a 24-year-old person as described in Lerman, S., Radiant Energy and the Eye, MacMillan, New York, 1980, P. 58, figure 2-21.
CRYSTALLINE LENS - Human crystalline lens from a 25-year-old person as described in Waxler, M., Hitchins, V.M., Optical Radiation and Visual Health, CRC Press, Boca Raton, Florida, 1986, p. 19, figure 5.

WARNING: UV-absorbing contact lenses are not substitutes for protective UV-absorbing eyewear such as UV-absorbing goggles or sunglasses. Persons should continue to use their protective UV-absorbing eyewear as directed.

NOTE: The effectiveness of wearing UV-absorbing contact lenses in preventing or reducing the incidence of ocular disorders associated with exposure to UV-light has not been established at this time.

## ACTIONS

Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy produce a temporary reduction of myopia by changing the shape (flattening) of the cornea, which is elastic in nature. Slightly reducing the curvature of the cornea reduces the excessive focusing power of the myopic 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.

Contact lenses rest directly on the corneal tear layer and can gently influence the corneal shape. Regular contact lenses are designed to cause little or no effect, but Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy are designed to purposely flatten the shape of the cornea by applying gentle pressure to the center of the cornea during sleep.

After the contact 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 Paragon Z CRT® lens design must be worn at night on a regular schedule to maintain the corneal reshaping, or the myopia will revert to the pretreatment level.

## INDICATIONS (USES)

Paragon Z CRT® (tisilfocon A) Rigid Gas Permeable Contact Lenses for Corneal Refractive Therapy are indicated for use in the reduction of myopic refractive error in nondiseased eyes. The lenses are indicated for overnight wear in a Corneal Refractive Therapy fitting program for the temporary reduction of myopia up to 6.00 diopters in eyes with astigmatism up to 1.75 diopters. The lenses may be disinfected using only a chemical disinfection system.

> Note: To maintain the Corneal Refractive Therapy 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 Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy when any of the following conditions exist:

- Acute and subacute inflammations or infection of the anterior segment 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 contact lenses.
- Any active corneal infection (bacterial, fungal or viral).
- If eyes become red or irritated.

## WARNINGS

Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy are shipped to the practitioner nonsterile. Clean and condition lenses prior to use.

Incorrect use of contact lenses and lens care products can result in serious injury to the eye. It is essential for the patient to follow the eye care practitioner's directions 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, or redness of the eye, instruct the patient to immediately remove the lenses and do not wear them until instructed to do so by the eye care practitioner. All contact lens wearers must see their eye care practitioner according to the schedule given to them.

Paragon Z CRT® Contact Lenses for Contact Lens Corneal Refractive Therapy 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 overnight Contact Lens Corneal Refractive Therapy prescribes only overnight wear with removal during the waking hours, and although the safety risks of intermittent overnight wear may not be as great as with sustained overnight wear; there is still increased risk beginning with the first overnight period.

> WARNING
> 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 of the lens 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.

Studies have shown that contact lens wearers who are smokers have a higher incidence of adverse reactions than nonsmokers.

## ADVERSE EFFECTS (PROBLEMS AND WHAT TO DO)

Patients should be informed that the following problems may occur.

- Eyes stinging, burning, itching (irritation), or other eye pain
- 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

If the patient notices any of these conditions, the patient should IMMEDIATELY REMOVE THE LENSES. The patient should 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 your eye. Place the lens in the storage case and contact your 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, you should thoroughly clean, rinse and disinfect the lens; then reinsert it.

- If the problem continues, you should IMMEDIATELY remove the contact lenses and consult your eye care practitioner.

When any of the above problems occurs, a serious condition such as infection, corneal ulcer, neovascularization, iritis, persistent stromal edema or GPC (giant papillary conjunctivitis) may be present. Instruct the patient 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.

**PRECAUTIONS**

Eye Care Practitioner

Clinical studies have demonstrated that Paragon Z CRT® contact lenses manufactured from Menicon Z® material are safe and effective for their intended use. However, due to the small number of patients enrolled in the clinical investigation of lenses, all refractive powers, design configurations, and lens parameters available in the lens materials were not evaluated in significant numbers. This is especially true for adolescent subjects in this investigation. Consequently, when selecting an appropriate lens design and parameters, the eye care practitioner should consider all characteristics of the lens that can affect lens performance and the patient's ocular health; including, oxygen permeability, wettability, central and peripheral thickness, and optic zone diameter.

The potential impact of these factors on the patient's ocular health should be carefully 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. Corneal edema is more prevalent when the lens is used in high altitudes.

Each Paragon Z CRT® lens is supplied nonsterile in an individual plastic case. The lens is shipped wet in Unique-pH® Multi-Purpose Solution. This solution contains hydroxypropyl guar, a unique wetting and conditioning polymer system, polyethylene glycol, Tetronic*, boric acid, propylene glycol; and, is preserved with POLYQUAD® (polyquarternium-1) 0.0011% and edetate disodium 0.01%. The case, packing slip or invoice is marked with the central base curve radius, dioptric power, overall diameter, Return Zone Depth, Landing Zone Angle, center thickness, serial number, ship date and the color of the lens. If the patient has experienced a prior history of allergy to any of these ingredients; remove the lens from the solution and soak the lens 24 hours in sterile unpreserved saline prior to cleaning, disinfecting and dispensing.

Unique-pH® is a Trademark of Alcon Laboratories, Inc.
* Registered Trademark of BASF corp.

Never reuse the solution. You may store the lens in the unopened container until ready to dispense, up to a maximum of twenty-five (25) days from the Ship Date (see Packing Slip). When a lens has been stored for 25 days in its original packaging solution, it should be cleaned and disinfected with an approved product (see recommended product list in the Lens Care Directions section), and placed into inventory as you presently do with any other RGP lens held in your office. Follow the directions on the selected disinfecting solution regarding prolonged storage.

Patient

Patients should be informed of the following precautions.

Solution Precautions

- Different solutions cannot always be used together, and not all solutions are safe for use with all lenses. Use only recommended solutions with the contact 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 your contact 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 and hands are free of foreign material before touching your contact lenses, as 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 eye care practitioner.
- Always handle your lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove your 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: Clean and condition lenses prior to use. Lenses come non-sterile.
- 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 nonmovement of the lens continues, you should immediately consult your eye care practitioner or attending hospital emergency room physician.
- 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 cases should be replaced at regular intervals as recommended by the lens case manufacturer or eye care practitioner.

Discuss these topics with each patient:

- Wear of contact lenses during sporting activities.
- Use of any medication in his or her eyes.
- Importance of adhering to the recommended follow-up schedule to assure the continuing health of his or her eyes.
- Inform your doctor (health care practitioner) about being a contact lens wearer.
- Inform your employer of being a contact lens wearer. Some jobs may require the use of eye protection equipment or may require that you not wear contact lenses during work hours.

**SUMMARY OF CLINICAL STUDY**

INTRODUCTION

Two hundred four eyes of 102 patients are presented in this report of a study of myopia and myopia astigmatism treatment with overnight wear of contact-lens corneal refractive therapy lenses in tisilfocon A material in a protocol controlled investigation at nine U.S. sites. The objective of this investigation was to determine the safety and effectiveness of the lenses in the population defined in the protocol. The corneal refractive therapy design used in this clinical trial gained FDA market approval on June 13, 2002 when manufactured in paflufocon B and paflufocon D.

DEMOGRAPHIC INFORMATION

The data presented in this report were collected and analyzed from the 204 eyes of 102 enrolled subjects of which 196 eyes of 98 subjects were treated at nine U.S. centers. The mean age of the full cohort of patients was 34.56 ± 11.6 years (range 11-57). There were 67 female and 31 male subjects enrolled and treated. The data for 72 patients (144 [1] eyes) were analyzed for effectiveness following 6 months of treatment. The mean age of these patients was 34.97 ± 12.0 years (range 11 to 57). A waiver was granted for one subject that was age 11 years 8 months at the baseline visit. There were 10 adolescent subjects enrolled, 2 withdrew prior to treatment. There were 48 female and 24 male subjects of these 47 were classified Caucasian, 3 were African American, 14 were Asian/Pacific Islander, 1 was American Indian/Aleut Eskimo, and 5 were classified Hispanic.

EFFECTIVENESS OUTCOMES

The average amount of myopia that can be expected to be corrected is shown in the following table. These values assessed on 137 eyes on which full correction was attempted are only averages and some patients can be expected to achieve more or less than these averages. Seven patients were given a monovision treatment in which one eye was targeted for emmetropia and one targeted to remain myopic, in order to provide near vision.

[1] At 1 month one subject converted to, and completed wearing only one lens.

AVERAGE REDUCTION IN MYOPIA (DIOPTERS) N=137*

| Refractive Range and Count | Average Subjective Refraction (MRSE) | Average Myopia Reduction (MRSE) | Average Residual Subjective Refraction (MRSE) |
|---|---|---|---|
| -0.25>-1.00 N=8 | -0.89 | 0.81+/ -0.48 | -0.08+/ -0.38 |
| -1.25>-2.00 N=40 | -1.63 | 1.49+/ -0.45 | -0.13+/ -0.40 |
| -2.25>-3.00 N=46 | -2.57 | 2.37+/ -0.62 | -0.20+/ -0.57 |
| -3.25>-4.00 N=25 | -3.67 | 3.23+/ -0.67 | -0.44+/ -0.62 |
| -4.25>-5.00 N=13 | -4.40 | 3.88+/ -0.67 | -0.52+/ -0.60 |
| -5.25>-6.00 N=5 | -5.50 | 5.65+/ -0.55 | 0.15+/ -0.55 |

*All completed eyes targeted for emmetropia.

Uncorrected Visual Acuity (UCVA)

Post treatment visual acuity was assessed on 137 eyes on whom full correction was attempted. Of these eyes 41.5% obtained 20/20 or better uncorrected visual acuity and 94.8% obtained 20/40 or better visual acuity at 6 months. See the following table.

Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy provided a temporary full reduction in some patients with up to -5.5 diopters of myopia. For patients with greater than -5.5 diopters of myopia only a partial reduction of myopia can be expected. The percentage of patients that can be expected to achieve full or partial temporary refractive reduction based on 144 [2] treated eyes is shown in the following table.

PERCENT OF COMPLETED EYES THAT ACHIEVED FULL OR PARTIAL TEMPORARY REDUCTION OF MYOPIA

| INITIAL MYOPIA | FULL REDUCTION ± 0.50 D from Target* | PARTIAL REDUCTION ± 1.00 D from Target* | FINAL V.A. 20/20 or better** | FINAL V.A. 20/40 or better** |
|---|---|---|---|---|
| 1.00 D or less | 88% | N/A | 50% | 100% |
| -1.25 to - 2.00 D | 83% | 100% | 60% | 95% |
| -2.25 to - 3.00 D | 81% | 95% | 39% | 93% |
| -3.25 to - 4.00 D | 70% | 93% | 24% | 92% |
| -4.25 to - 5.00 D | 79% | 86% | 23% | 100% |
| -5.25 to -6.00 D | 33% | 83% | 33% | 100% |

* N=144 for reduction (all efficacy qualified eyes)

** N=137 for Final VA (only eyes targeted for emmetropia)

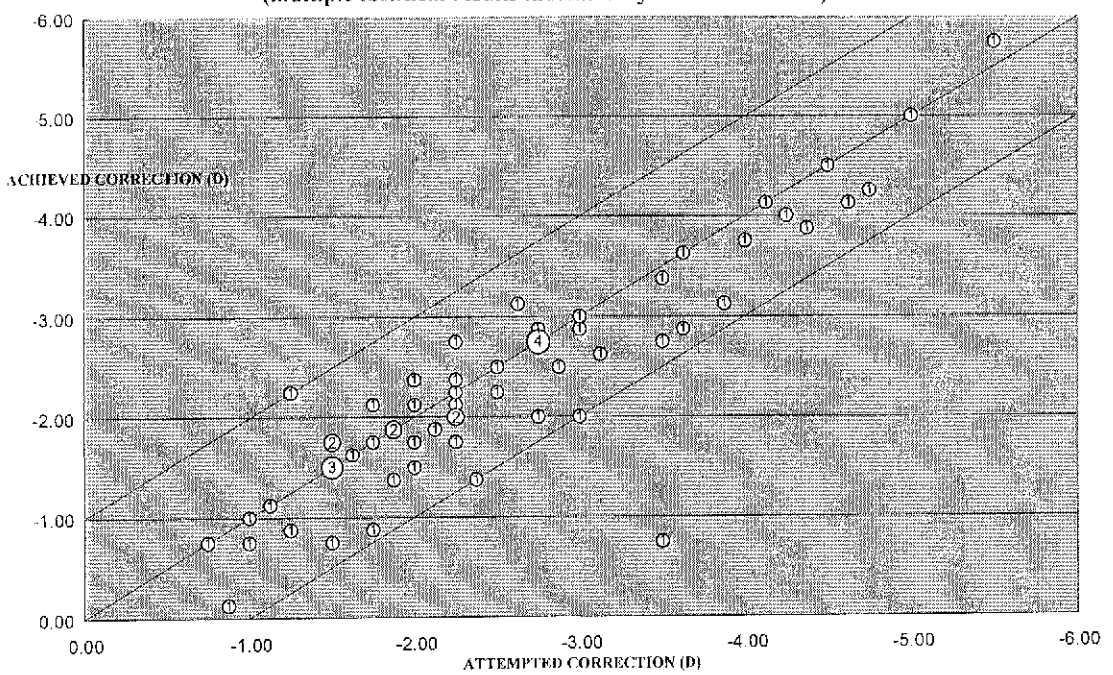
[2] At 1 month one subject converted to, and completed wearing only one lens.

Accuracy

Accuracy of outcome was evaluated by analysis of attempted versus achieved manifest refraction spherical equivalent. At the 6-month visit, 77.6% (111/144 [3]) of 6-month completed eyes were within 0.50 D attempted spherical equivalent correction, and 95.1% (136/144) of eyes were within 1.00 D of attempted correction. In this clinical study the higher the initial myopia the lower the percentage of patients achieved full correction and/or 20/20 vision. The preceding table demonstrates the relationship of initial myopia with treatment success.

There is reference in a published study [4] regarding visual acuity in the "better seeing eye" of a subject as a useful method of estimating functional vision when using both eyes. Of course, very few patients need to rely on the vision from a single eye. When the study subjects were analyzed for only their "better seeing eye", 86% had 20/20 or better vision, and 100% had 20/40 or better. The accuracy calculation also changes slightly. 80% Are estimated to be within 0.5 D of target; 96% are estimated to be within 1.0 D of target in keeping with the method of better eye analysis. The scatter plot below graphically depicts the accuracy of the treatment based on the better seeing eye.

**ATTEMPTED versus ACHIEVED Correction of Refractive Error**
**Estimated From The Residual Error Of the Better Seeing Eye, N=65***
**(multiple identical results indicated by number in circle)**




* Excludes 7 subjects not targeted for emmetropia in both eyes.

[3] At 1 month one subject converted to, and completed wearing only one lens.

[4] Monocular Versus Binocular Visual Acuity as Measures of Vision Impairment and Predictors of Visual Disability, Rubin, et al, Invest Ophthalmol Vis Sci 2000; 41:3327-3334

Wearing Time

The lenses were used for overnight wear only. They were applied within 30 minutes of sleep and removed within 30 minutes of awakening. The average wearing time was 6 to 8 hours and reflected the expected distribution of night-sleep time. There was no apparent relationship between the number of hours of wear during sleep and the visual acuity outcome for any amount of pretreatment myopia.

Regression Of Visual Acuity

To help you assess the change over time following lens removal, subjects in the clinical study were evaluated at 8, 24, 48, and 72 hours after removal of their lenses following either the six or nine month scheduled visit. Remember that the times given are averages, many patients will do better, many will not fare as well. The 1 Diopter regression point was chosen because it approximately corresponds to 20/40 unaided vision, the legal requirement for driving in many states.

The following guidance table is intended for counseling patients regarding the stability of their vision throughout the day. Values in the table represent the number of hours from the time of lens removal before the average patient's vision will have regressed to the point that his refraction is -1.0 Diopter (roughly corresponding to 20/40).

To use the chart, find the patient's original pretreatment manifest refractive spherical equivalent (MSRE) in the 3rd horizontal row then move down that column to the row where the refraction (in column 2) matches the refraction your patient achieves immediately on lens removal after a night's wear. The bold value found in the cell identified in this way represents the average number of hours that similar patients have experienced before their refractive error has regressed to approximately -1.0 Diopter. Beneath that value is the minimum projected time for any subject in the study. This is only a guideline; every patient should test his/her vision as it relates to the requirements of their own daily schedules.

BE SURE TO MAKE YOUR PATIENTS AWARE OF THESE LIMITATIONS OF CORNEAL REFRACTIVE THERAPY AND THE OPTIONS AVAILABLE TO THEM WHEN A PROBLEM ARISES.

**AVERAGE AND MINIMUM HOURS UNTIL REGRESSION TO -1.0 DIOPTER OR WORSE**

**(estimated for all subjects with pretreatment MRSE > -1.0 D targeted for emmetropia and corrected to better than -1.0 D MRSE N=79)**

| REFRACTION AT LENS REMOVAL | | | -1.12 to -2.00 | -2.12 to -3.00 | -3.12 to -4.00 | -4.12 to -5.00 | -5.12 to -6.00 |
|---|---|---|---|---|---|---|---|
| | +0.50 | **Mean** | **163.7 Hrs** | **52.6 Hrs** | **19.8 Hrs** | **12.1 Hrs** | **16.9 Hrs** |
| | | Minimum | 9.3 Hrs | 3.7 Hrs | 4.3 Hrs | 5.3 Hrs | 5.5 Hrs |
| | +0.25 | **Mean** | **162.3 Hrs** | **51.6 Hrs** | **18.9 Hrs** | **11.4 Hrs** | **15.9 Hrs** |
| | | Minimum | 9.3 Hrs | 3.5 Hrs | 4.1 Hrs | 4.9 Hrs | 5.1 Hrs |
| | 0.00 | **Mean** | **159.4 Hrs** | **49.9 Hrs** | **17.5 Hrs** | **10.5 Hrs** | **14.4 Hrs** |
| | | Minimum | 9.2 Hrs | 3.2 Hrs | 3.9 Hrs | 4.4 Hrs | 4.7 Hrs |
| | -0.25 | **Mean** | **153.5 Hrs** | **46.9 Hrs** | **15.5 Hrs** | **9.1 Hrs** | **12.3 Hrs** |
| | | Minimum | 9.1 Hrs | 2.8 Hrs | 3.4 Hrs | 3.8 Hrs | 4.1 Hrs |
| | -0.50 | **Mean** | **139.7 Hrs** | **41.1 Hrs** | **12.3 Hrs** | **7.1 Hrs** | **9.5 Hrs** |
| | | Minimum | 8.5 Hrs | 2.2 Hrs | 2.8 Hrs | 2.9 Hrs | 3.1 Hrs |
| | -0.75 | **Mean** | **103.9 Hrs** | **28.8 Hrs** | **7.5 Hrs** | **4.3 Hrs** | **5.5 Hrs** |
| | | Minimum | 5.1 Hrs | 1.2 Hrs | 1.6 Hrs | 1.6 Hrs | 1.8 Hrs |

Effects On Astigmatism

Corneal Refractive Therapy does not predictably affect the magnitude of pretreatment astigmatism. Either increases or decreases in astigmatism may occur following Contact Lens Corneal Refractive Therapy. Of the eyes that completed the nine-month clinical study, 27% showed no change in refractive astigmatism, 49% showed a decrease of one diopter or less and 1% showed a decrease more than one diopter, while 23% showed an increase of one diopter or less and 1% showed an increase greater than one diopter of refractive astigmatism.

**OVERNIGHT WEAR SAFETY SUMMARY**

In this trial, 196 eyes from 98 patients were evaluated for safety during six months overnight wear corneal refractive therapy when treating myopia and myopia with astigmatism. . In this study analysis of safety outcomes was performed for BSCVA losses, adverse events, complications, intraocular pressure, slit lamp findings and symptoms problems and complaints. The analysis was completed for all eyes that reported at all visits.

Best Spectacle-Corrected Visual Acuity (BSCVA)

The BSCVA change analyzed in this trial is the difference between the baseline acuity with best subjective refraction and the acuity with the subjective refraction at the specified visit.

Seventy percent of completed eyes (101/144 [5]) experienced no change in BSCVA at 6 months, while 15 % (22/144) experienced one line of improved BSCVA and 10% (14/144) eyes experienced on line of diminished BSCVA. Five completed eyes, 3.5% (5/144) manifested a transient loss of two or more lines of BSCVA at the six-month visit. All losses except one were found to be transient as they were not found to be present at the post-removal visits. In one case recovery was not documented before the eye was lost to follow-up. There was one eye with BSCVA worse than 20/40 at the six month visit. At prior visits, with the exception of 3 cases, eyes measuring worse than 20/40 BSCVA were re-tested with a contact lens in place. In those cases retested with a lens, the acuity improved to within one line of vision, indicating that the loss was due to higher order aberration in the anterior corneal plane. In the cases when the test was mistakenly omitted the BSCVA loss improved to within one line of vision by the next scheduled visit. There is a pattern of transient BSCVA loss at each visit and a trend toward a decreasing percentage with time.

After passing the dispensing and a successful day one visit, of the 204 eyes originally enrolled in the study, 35 were found, at one point or another, to have temporarily lost 2 lines or more of BSCVA from baseline. In one case recovery was not documented before the eye was lost to follow-up. Additionally, eight subjects were observed to temporarily have BSCVA's of 20/40 or worse.

Absence of Persistent Corneal Change

The protocol stipulates that all treated eyes of subjects who discontinued the clinical trial must be followed one month post discontinuation and every one month thereafter until there was no difference greater than 0.50 D in either of the keratometric meridians from the baseline measures. Of the 58 discontinued eyes of the 29 discontinued subjects, 39 eyes of 20 subjects were within 0.50 D of the baseline measurements at the discontinuation visit. One of the discontinued subjects (2 eyes) was lost to follow-up during the investigation. Eleven eyes of 6 subjects were measured to be within 0.50 D of their baseline visit at a post discontinuation visit. Two enrolled subjects were not dispensed.

[5] At 1 month one subject converted to, and completed wearing only one lens.

Slit Lamp Findings

There were no grade 2 or 3 observations at baseline. There were 1578 observations for all scheduled and unscheduled follow up visits. There were 61 grade 2 (mild) observations (3.9%) during treatment and 7 grade 3 (moderate) observations (< 0.5%) reported. There were no grade 4 (severe) observations reported that would constitute adverse events.

Of the 8 grade 3 reports five were for staining, one for injection and two were for other and described as corneal infiltrates. All 8 cases resolved without further complication. These occurred in 4 subjects. In each case lens wear was discontinued. Two subjects discontinued the study and 2 completed. All cases resolved without further complication.

Symptoms, Complaints and Discontinuations

One hundred two subjects underwent baseline evaluation in the study. Of these, 98 subjects (196 eyes) had lenses dispensed and wore them for at least one night of treatment. The safety analysis was conducted on all 196 treated eyes of the 98 subjects. Seventy-two subjects, 73.5% (144 [6]/196 eyes), completed six months of treatment. The efficacy analysis was conducted on all 72 subjects (144 eyes) that completed six months of treatment. Of the 98 subjects, 29 were discontinued prior to the six-month visit. The table below reports the tabulation of subjects that were discontinued prior to the six-month visit and the reason for discontinuation.

| **Reason for Discontinuation (N=102 enrolled subjects)** | |
|---|---|
| Reason for Discontinuation | Number of Patients |
| Unacceptable Visual Acuity | 13 |
| Other | 6 |
| Lack of Comfort | 3 |
| Lack of Interest | 5 |
| Protocol Violation | 2 |
| Missed Visits | 0 |
| Pathology | 0 |

The reasons given for "other" include two subjects who reported lens adherence, one that reported "lens slipping" at night, one who had back surgery and could not attend visits, and two not dispensed. The protocol violation listing includes two subjects who stopped wear of the lenses for long periods during the study.

The clinical reasons for discontinuation are unacceptable vision, lack of comfort, lens adherence and lens slipping that account for 13 % (13/98), 3 % (3/98), 2% (2/98) and 1% (1/98) respectively. The total discontinuation rate for clinical reasons was 19 %.

[6] At 1 month one subject converted to, and completed wearing only one lens.

| PERCENT OF EYES EXHIBITING COMPLAINT OR SYMPTOM AT VISIT | | | | | | |
|---|---|---|---|---|---|---|
| Visit | Unscheduled | 2-Week | 1-Month | 2-Month | 3-Month | 6-Month |
| Total Eyes at Visit | 260 | 168 | 158 | 164 | 160 | 144 |
| None | 39% | 44% | 63% | 68% | 69% | 81% |
| Discomfort | 24% | 20% | 15% | 14% | 15% | 8% |
| Itching/Burning | 6% | 4% | 0% | 4% | 1% | 0% |
| Blurred Vision | 26% | 20% | 8% | 4% | 4% | 5% |
| Dryness/Scratch | 6% | 3% | 6% | 7% | 3% | 5% |
| Redness | 5% | 2% | 1% | 0% | 0% | 0% |
| Variable Vision | 12% | 15% | 4% | 2% | 4% | 3% |
| Photophobia | 3% | 1% | 0% | 0% | 1% | 0% |
| Halos | 4% | 11% | 8% | 5% | 3% | 1% |
| Ghost Images | 0% | 1% | 1% | 1% | 0% | 1% |
| Lens Adhesion | 5% | 2% | 1% | 0% | 1% | 1% |
| Lens Need Cleaning | 2% | 5% | 1% | 3% | 0% | 1% |
| Other | 6% | 3% | 1% | 1% | 0% | 2% |

Adverse Events and Complications

Study related complications were reported, along with other clinical findings throughout the course of the study. Investigators were encouraged to report all clinical findings, regardless of severity or frequency. As these events were brought to the attention of the study monitors, appropriate information was examined regarding the treatment and post-treatment course of each individual eye. Often this information included but was not limited to BSCVA, UCVA, refraction, slit lamp findings and videokeratography.

These reports were followed up, where necessary, with a phone call to the investigator. One subject was found to have suffered a loss of greater than 2 lines of acuity from his baseline BSCVA and it was lost to follow-up. Although recovery was not documented, this subject had no significant ocular pathology observed at any visit. Another subject was found to have similar a loss and was not documented to have recovered for 216 days. One subject experienced a loss of acuity in one eye to worse than 20/40 whose recovery was not documented for 89 days.

There were three events reported on Adverse Event Forms. Two were rated as moderate and one as mild. No serious adverse events were reported.

The following is the description of the adverse events. One subject experienced a peripheral corneal infiltrate, discontinued lens wear, administered medication, and the infiltrate resolved in 7 days. A second subject experienced two incidents of corneal infiltrates, discontinued lens wear, administered medication, and each occurrence resolved in 6 days.

Lens adherence was reported in two subjects who discontinued and was listed as a study related complication. It was also reported as a symptom, problem or complaint. There were twenty one positive reports of lens adherence in thirteen eyes of nine subjects. The right eye of one subject was the only eye to report persistent lens adherence (at multiple sequential visits). It is noteworthy that this eye was also reported to have a moderate adverse event.

There were no slit lamp findings graded at level 4 (severe). All grade 2 or greater measures resolved without complication. The remaining study related complications were restricted to the transient losses of two or more lines of BSCVA, reductions to $\leq$ 20/40 and to slit lamp findings graded at level 3 (moderate). For subjects completing at least a day 1 visit there were 63 occurrences in 50 eyes of temporary loss of 2 or more lines of visual acuity. Of 186 subject eyes that continued to scheduled visits beyond day 1, and excluding observations at day 1 visits, there were 35 occurrences of temporary loss of 2 or more lines of visual acuity.

Of these occurrences 15 occurred on scheduled visits beyond the early fitting period*, and 7 were at Unscheduled or Discontinuation visits. The average duration for all occurrences until the investigator was able to bring the subject in and document recovery to better than 2 lines from baseline was 31.4 days. Although the range of durations until documented recovery** was 0 to 216 days (one subject could not be returned for documentation), the median duration was 18 days. Of the 15 occurrences beyond the early fitting period none were bilateral and the average logMAR acuity at the time of the first observation was 0.17 (better than 20/32 in that eye). Only two of these eyes demonstrated visual acuities worse than 20/40 when first observed and they were documented to have been resolved at their next follow-up visit in 7 and 21 days respectively.

*Period from dispense through successful 2-week visit
**Actual Recovery may have occurred earlier

Eight subjects presented with acuities of $\leq$ 20/40 during the course of the study. Two were observed only at the day 1 visit. One subject placed lens cleaner in his eye just after the 3-month visit but was not documented to have recovered until the 6-month visit, 89 days later. Excluding the subject who put cleaner in his eye, the range for time to documented recovery was 0.3 – 21 days with a median of 11days.

There were no slit lamp findings graded at level 4 (severe). All grade 2 or greater measures resolved without complication.

Three subjects (5 eyes) experienced grade 3 staining. No subjects with grade 3 staining required antibiotic treatment or lens wear discontinuation equal to two weeks. The table below summarizes the findings related to these events.

| Eye | Date | Visit | Treatment for Grade 3 Staining |
|---|---|---|---|
| OD | 06/10/04 | Two Wk | Discontinued Lens Wear for 6 Days |
| OS | 06/10/04 | Two Wk | Discontinued Lens Wear for 6 Days |
| OD | 05/27/04 | Day One | Discontinued Lens Wear for 24 Hours |
| OD | 07/15/04 | Day One | Not Contact Lens Related - Discontinued Lens Wear for 1 Week |
| OS | 07/15/04 | Day One | Not Contact Lens Related - Discontinued Lens Wear for 1 Week |

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

**Summary of Key Safety Variables ***

| Criteria | 1 Day | | 2 Weeks | | 1 Month | | 2 Months | | 3 Months | | 6 Months | | Unscheduled** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % | n | % | n | % |
| n | 196 | | 168 | | 158 | | 164 | | 160 | | 144 | | 210 | |
| Adverse events | | | | | | | | | | | | | 3 | 1.4 |
| Loss of ≥ 2 lines BSCVA*** | 32†† | 16.3 | 9 | 5.4 | 4 | 2.5 | 2 | 1.2 | 4 | 2.5 | 5 | 3.5 | 7 | 3.3 |
| BSCVA worse than 20/40 *** | 4 | 2.0 | 3 | 1.8 | 1 | 0.6 | 0 | 0 | 1 | 0.6 | 1 | 0.7 | 2 | 1.0 |
| Increase of > 1 D Refractive Cyl | 2 | 1.0 | 4 | 2.4 | 2 | 1.3 | 1 | 0.6 | 0 | 0 | 0 | 0 | 6 | 2.9 |
| Increase of > 2 D Refractive Cyl † | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Increase of > 1 D Corneal Cyl | 16 | 8.2 | 8 | 4.8 | 5 | 3.2 | 7 | 4.3 | 12 | 7.5 | 10 | 6.9 | 12 | 5.7 |
| Increase of > 2 D Corneal Cyl † | 0 | 0 | 4 | 2.4 | 0 | 0 | 2 | 1.2 | 3 | 1.9 | 1 | 0.7 | 0 | 0 |

* Includes multiple interim observations of some events.

** Includes Discontinuation visits and regression study visits.

*** There were 35 incidents of loss ≥ 2 lines of vision (all documented to be temporary except one).

† All cylinder increases of ≥ 2 Diopters were temporary.

†† On the 32 day-one observations, 4 of these observations were still observed at the 2-week visit (in addition to the 9 new cases at 2 weeks noted in the table).

Patient Satisfaction

Fifty-nine of the 72 completed subjects (85.3%) rated their overall satisfaction with their unaided vision equivalent to very good or excellent at the 6 month visit compared to no subjects (0.0%) for the same equivalent rating pretreatment.

## FITTING

NOTE: Contact lenses for Corneal Refractive Therapy should be fitted only by a contact lens fitter trained and certified in the fitting of conventional and sigmoid geometry contact lenses.

Conventional methods of fitting rigid contact lenses DO NOT APPLY to the Paragon Z CRT® Contact Lenses for Contact Lens Corneal Refractive Therapy. For a description of fitting techniques, refer to the Professional Fitting And Information Guide – Paragon Z CRT®. Copies are available from:

Paragon Vision Sciences, Inc.
947 E. Impala Avenue
Mesa, Arizona 85204-6619

## RECOMMENDED INITIAL 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 recommended by the eye care practitioner regardless of how comfortable the lenses feel.

It is ideal for the patient to start with overnight wear the first night. A well fit lens provides for centration with the closed eye. The effects of lid interaction on blinking and gravity may result in lens decentration during

open eye wear. Patients should be instructed to place the lens in the eye 15 to 20 minutes before going to sleep.

Patients must be cautioned; "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, the patient should be instructed to remove the lens, clean and rewet it and replace the lens. If the sensation continues, the lens should not be worn.

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 the lens 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 lens until the next scheduled follow-up visit.

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

| | |
|---|---|
| Day 1 | two periods of wear not to exceed 6 hours total |
| Day 2 | 6 hours |
| Day 3-5 | 8 hours |
| Day 6 | overnight wear with follow-up visit within 24 hours |

The cornea normally changes within five to eight hours of wear. The wearing schedule should be modulated to determine the MINIMUM wear required for myopic reduction. The average wearing time is between 8 and 10 hours. Determine the wearing time at which lens movement appears to stop. Attempt to maintain wearing time at this level.

## MYOPIC REDUCTION MAINTENANCE LENS (RETAINER LENS) WEARING SCHEDULE

With Paragon Z CRT® contact lenses, the lens used to achieve refractive therapy is usually the lens used to maintain achieved correction. The Retainer Lens wearing time begins with the same wearing time required for the last fitted Paragon Z CRT® Contact Lenses for Contact Lens Corneal Refractive Therapy. After a period of several days, or when the eye care practitioner is satisfied that the patient has adapted to the first Retainer Lenses, the patient may attempt to skip a night of wear to monitor the duration of visual improvement. This may continue for 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.

Note: To maintain the Contact Lens Corneal Refractive Therapy 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.

## LENS CARE DIRECTIONS

The following is a list of products available for use with Paragon Z CRT® rigid gas permeable contact lenses. This is not an exclusive list. You may use other lens care solutions as recommended by your eye care practitioner.

| | |
|---|---|
| Cleaning | Unique-pH® Multi-Purpose Solution, SupraClens®, Opti-Clean® II, ProFree/GP® |
| Disinfection | Unique-pH® Multi-Purpose Solution, Wet-N-Soak® Plus, Barnes-Hind® ComfortCare GP Wetting and Soaking Solution |
| Lubrication | Clerz® Plus |

PRODUCT LIST

Unique-pH® Multi-Purpose Solution, SupraClens®, Opti-Clean® II, Clerz® Plus by Alcon Laboratories, Inc.

ProFree/GP®, Wet-N-Soak® Plus, Barnes-Hind® ComfortCare GP Wetting and Soaking Solution by Advanced Medical Optics (AMO)

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 the disinfection and storage systems unless so indicated on the product label.

Inform the patient of the following lens care suggestions.

- Always wash and rinse your hands thoroughly before handling your contact lenses.
- Never use tweezers or other tools to remove your lens from the lens container. Pour the lens into your hand.
- Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy 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.
- Clean one lens first. The recommended procedure is to always clean the same lens first to avoid mix-ups. Rinse the lens thoroughly to remove the cleaning solution. Place the lens into the correct storage chamber and fill the chamber with the recommended disinfection system as recommended by your eye care practitioner. Clean and rinse the other lens in the same manner and place it in its chamber.
- 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 unopened storage case until you are ready to put them in your eye.

**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 lens case manufacturer, and allowed to air dry. Lens cases should be replaced at regular intervals as recommended by the eye care practitioner.

**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**

CAUTION: Nonsterile lenses. Clean and condition lenses prior to use.

Each Paragon Z CRT® lens is supplied nonsterile in an individual plastic case. The lens is shipped wet in Unique-pH® Multi-Purpose Solution. This solution contains hydroxypropyl guar, a unique wetting and conditioning polymer system, polyethylene glycol, Tetronic*, boric acid, propylene glycol; and, is preserved with POLYQUAD® (polyquarternium-1) 0.0011% and edetate disodium 0.01%. The case, packing slip or invoice is marked with the central base curve radius, dioptric power, overall diameter, Return Zone Depth, Landing Zone Angle, center thickness, serial number, ship date and the color of the lens. If the patient has experienced a prior history of allergy to any of these ingredients; remove the lens from the solution and soak the lens 24 hours in sterile unpreserved saline prior to cleaning, disinfecting and dispensing.

Unique-pH® is a Trademark of Alcon Laboratories, Inc.
* Registered Trademark of BASF corp.

Never reuse the solution. You may store the lens in the unopened container until ready to dispense, up to a maximum of twenty-five (25) days from the Ship Date (see Packing Slip). When a lens has been stored for 25 days in its original packaging solution, it should be cleaned and disinfected with an approved product (see recommended product list in the Lens Care Directions section), and placed into inventory as you presently do with any other RGP lens held in your office. Follow the directions on the selected disinfecting solution regarding prolonged storage.

**REPORTING OF ADVERSE REACTIONS**

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

Paragon Vision Sciences, Inc.
947 E. Impala Avenue
Mesa, Arizona 85204-6619

www.paragoncrt.com

1-800-528-8279
1-480-892-7602
1-480-926-7369 FAX

*APPROPRIATE TEXT CODE*

# Considering Contact Lens Corneal Refractive Therapy?

**Patient Information Booklet for Potential Users of**
**Paragon Z CRT®**
**Contact Lenses for Contact Lens Corneal Refractive Therapy**

**PATIENT INFORMATION BOOKLET**
**FOR POTENTIAL USERS OF**

# Paragon Z CRT®

Manufactured in Menicon Z® (tisilfocon A)

## Contact Lenses For
## Contact Lens Corneal Refractive Therapy

## Overnight Wear

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

Contact lenses for Corneal Refractive Therapy should be fitted only by a contact lens fitter trained and certified in the fitting of conventional and sigmoid geometry contact lenses.

## TABLE OF CONTENTS

## INTRODUCTION

The information in this booklet is to help you decide whether or not to be fitted with Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy. Contact Lens Corneal Refractive Therapy is a fitting procedure that temporarily corrects or greatly reduces nearsightedness (myopia) with or without astigmatism after contact lenses have been removed. By temporary, it is meant that the contact lenses are worn while sleeping (overnight) and then removed upon awaking; whereupon the nearsightedness remains corrected or greatly reduced for all or most of your waking hours. The exact time period over which the myopia remains corrected varies with each patient. Generally, Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy must be worn each night to maintain the effect.

Note: Contact lenses for Corneal Refractive Therapy should be fitted only by a contact lens fitter trained and certified in the fitting of conventional and sigmoid geometry contact lenses.

## HOW THE EYE FUNCTIONS

The eye is very much like a camera and must be in good focus to see objects clearly. The focusing power of the eye comes from two eye structures, the cornea and the lens (Figure 1).

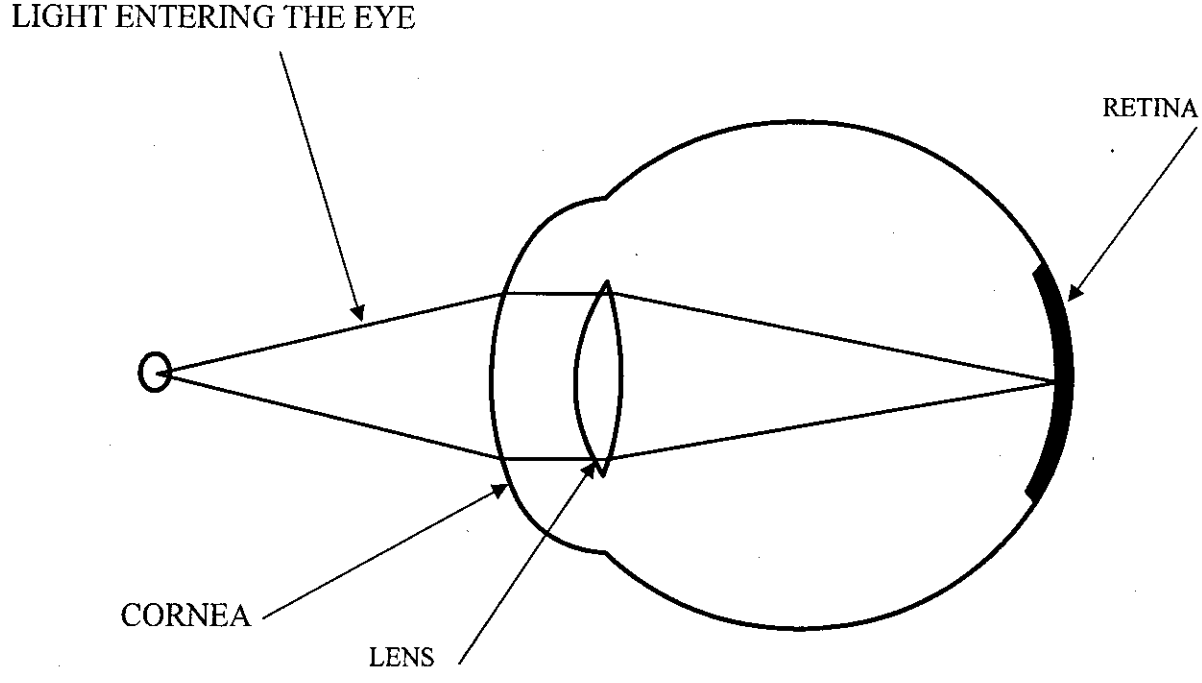



Figure 1: Normal Eye

The cornea is the clear, bubble-like structure on the front of the eye, where light first enters the eye. It provides about two-thirds of the eye's focusing power, and the lens inside the eye provides the other third. In a normal eye light focuses at the retina, at the back of the eye, which acts like the film in a camera.

Some eyes focus, or refract, the light too much, so that the images of distant objects are formed in front of the retina, and the image on the retina is blurred, producing myopia (Figure 2).

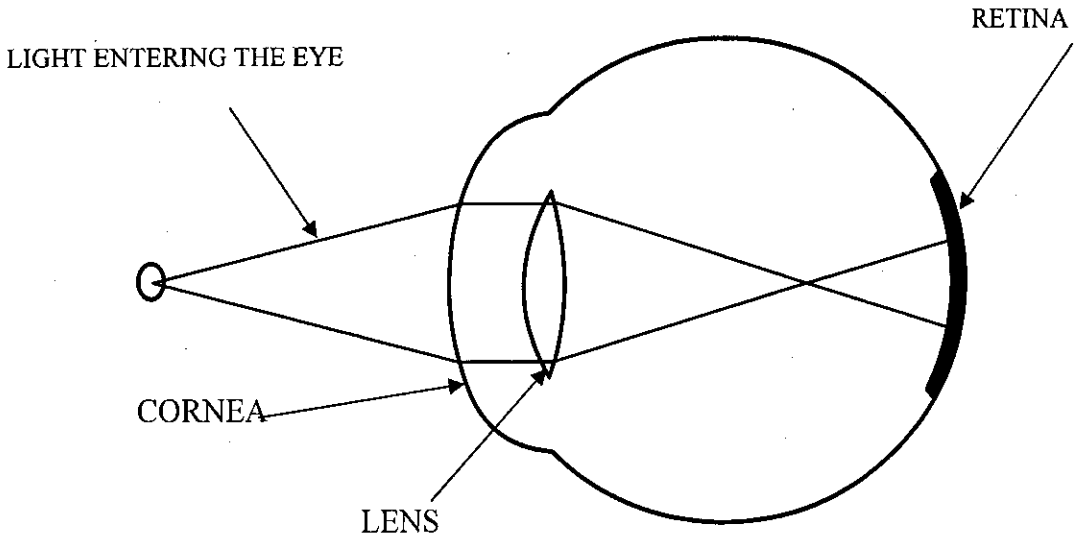



Figure 2: Nearsighted Eye

Myopia usually starts in childhood and gets progressively worse through adolescence. It normally stops increasing by the late teens, but it may sometimes continue to get worse into the mid-twenties.

**HOW PARAGON Z CRT® CONTACT LENSES FOR CORNEAL REFRACTIVE THERAPY FUNCTION**

These contact lens designs for Corneal Refractive Therapy produce a temporary reduction of nearsightedness by changing the shape (by flattening) of the cornea, which is elastic in nature. Contact lenses rest gently on the cornea, separated only by a layer of tears, and can influence the corneal shape. Regular contact lenses are designed to nearly match the shape of the cornea and thereby cause little or no flattening effect.
Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy are designed purposely not to match the shape of the cornea, but instead to apply slight pressure to the center of the cornea (Figure 3).

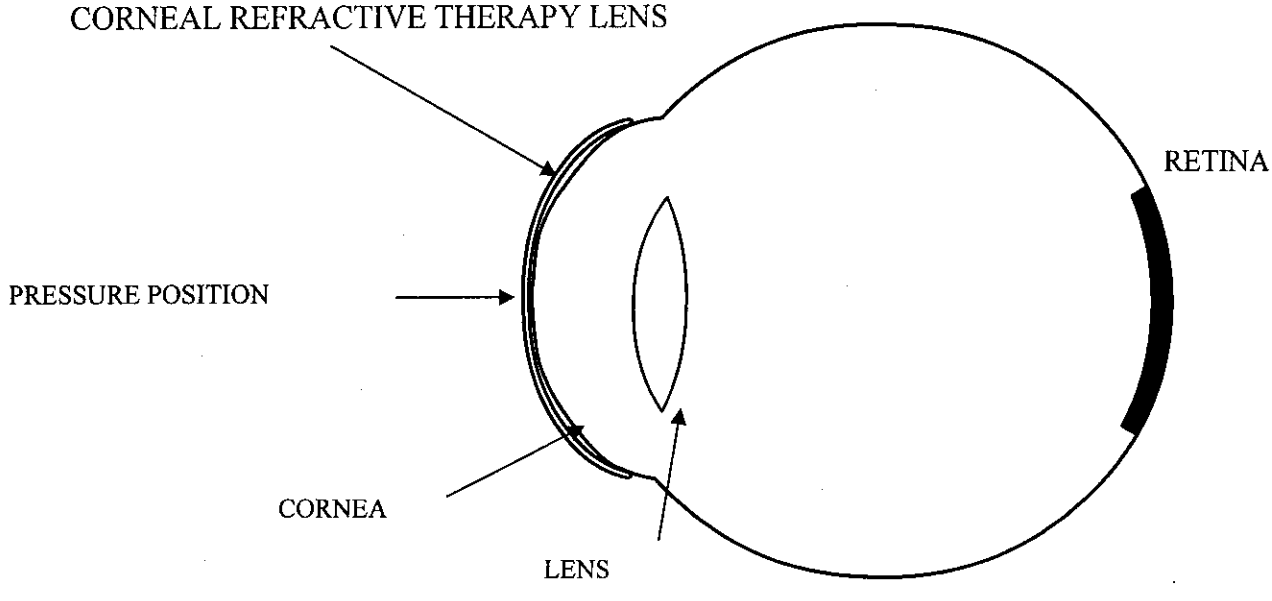



Figure 3: Eye Fitted With The CRT® Contact Lens Design For Corneal Refractive Therapy



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Pressure is produced when the lens is less curved than the cornea, which places more of the lens weight on the center of the cornea.

If the cornea is flattened this reduces the focusing power of the eye, and if the amount of corneal flattening is sufficient, it is possible to bring the eye into correct focus and compensate for myopia (Figure 4).

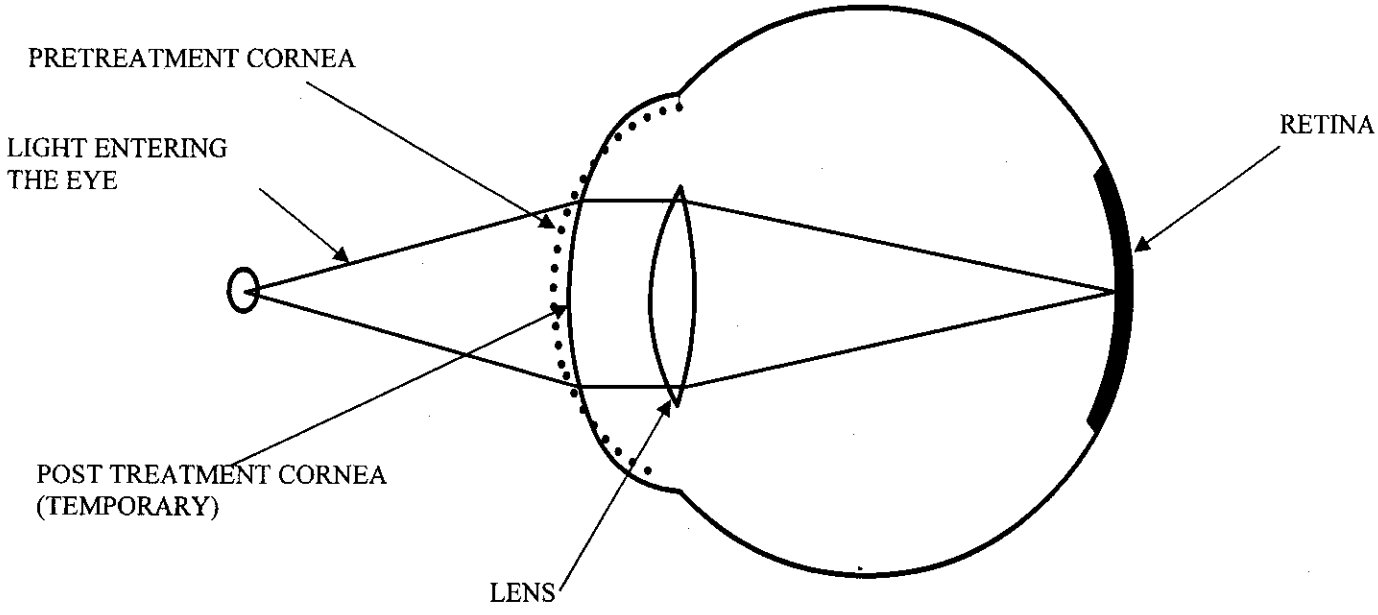


Figure 4: Nearsighted Eye After Contact Lens Corneal Refractive Therapy

Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy are generally worn overnight. After the lens is removed, the cornea retains its altered shape and corrected focus for all or most of your waking hours.

These contact lenses for Corneal Refractive Therapy are indicated for patients who want to see clearly during their daily activities, free from the inconvenience of traditional of contact lenses or spectacles. Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy may also be indicated for occupations that require exposure to smoke, noxious gases or conditions of low humidity.

These contact lenses for Corneal Refractive Therapy produce a temporary reduction of all or part of your myopia. The amount of reduction will depend on many factors, including the amount of your initial myopia, the elastic characteristics of your eye and the way that the contact lens fits on your eye.

**ALTERNATIVE WAYS TO CORRECT NEARSIGHTEDNESS**

Nearsightedness (myopia) can be corrected by any method that reduces the focusing power of the eye. The most common alternative methods are eyeglasses or regular daily wear or extended wear contact lenses. These represent a means of correcting myopia only during the time that the eyeglasses or regular contact lenses are worn, with no lasting effect on the myopia. Other methods of correcting myopia involve various surgical procedures such as LASIK.

**RISK ANALYSIS**

There is a small risk involved when any contact lens is worn. It is not expected that Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy will provide a risk that is greater than other rigid gas permeable contact lenses.

The two most common side effects, which occur in rigid contact lens wearers are corneal edema (swelling) and corneal staining (e.g. abrasion). It is anticipated that these two side effects will also occur in some wearers of Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy. Other side effects, which sometimes occur in all rigid contact lens wearers are pain, redness, tearing, irritation, discharge, abrasion of the eye or distortion of vision. These are usually temporary conditions if the contact lenses are removed promptly and professional care is obtained. When overnight Corneal Refractive Therapy lenses dislocate during sleep, transient distorted vision may occur the following morning after removal of the lenses. This distortion may not be immediately corrected with spectacle lenses. The duration of distorted vision would rarely be greater than the duration of the daily visual improvement normally achieved with the lenses.

In rare instances, there may occur permanent corneal scarring, decreased vision, infections of the eye, corneal ulcer, iritis, or neovascularization. The occurrence of these side effects should be minimized or completely eliminated if proper schedule of care is followed. You should remove your contact lenses if any abnormal signs are present.

**INDICATIONS**

Paragon Z CRT® (tisilfocon A) Rigid Gas Permeable Contact Lenses for Corneal Refractive Therapy are indicated for use in the reduction of myopic refractive error in nondiseased eyes. The lenses are indicated for overnight wear in a Corneal Refractive Therapy fitting program for the temporary reduction of myopia up to 6.00 diopters in eyes with astigmatism up to 1.75 diopters. The lenses may be disinfected using only a chemical disinfection system.

Note: To maintain the Corneal Refractive Therapy 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.

**PRECAUTIONS**

General

Clinical studies have demonstrated that Paragon Z CRT® contact lenses manufactured from Menicon Z® are safe and effective for their intended use. However, due to the small number of patients enrolled in the clinical investigation of lenses, all refractive powers, design configurations, and lens parameters available in the lens materials were not evaluated in significant numbers. This is especially true for adolescent subjects in this investigation. Consequently, when selecting an appropriate lens design and parameters, the eye care practitioner should consider all characteristics of the lens that can affect lens performance and your ocular health; including, oxygen permeability, wettability, central and peripheral thickness, and optic zone diameter.

The potential impact of these factors on your ocular health should be carefully weighed against your need for refractive reduction; therefore, your continuing ocular health and lens performance on the eye should be carefully monitored by your prescribing eye care practitioner. Corneal edema is more prevalent when the lens is used in high altitudes.

Each Paragon Z CRT® lens is supplied nonsterile in an individual plastic case. The lens is wet shipped in Unique-pH® Multi-Purpose Solution. This solution contains hydroxypropyl guar, a unique wetting and conditioning polymer system, polyethylene glycol, Tetronic*, boric acid, propylene glycol; and, is preserved with POLYQUAD® (polyquarternium-1) 0.0011% and edetate disodium 0.01%. If you have experienced a prior history of allergy to any of these ingredients, remove the lens from the solution and soak the lens 24 hours in sterile unpreserved saline prior to cleaning, disinfecting and dispensing.

* Registered Trademark of BASF corp.
Unique-pH® is a Trademark of Alcon Laboratories, Inc.

Never reuse the solution. You may store the lens in the unopened container until ready to dispense, up to a maximum of twenty-five (25) days from the Ship Date (see Packing Slip). When the lens has been stored for 25 days in its original packaging solution, it should be cleaned and disinfected with an approved product. Follow the directions on the selected disinfecting solution regarding prolonged storage.



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Patient

You should be aware of the following precautions.

Solution Precautions

- Use only recommended solutions with the contact lenses. Different solutions cannot always be used together, and not all solutions are safe for use with all 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 your contact 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 your hands before handling lenses. Do not get cosmetics, lotions, soaps, creams, deodorants, or sprays in your eyes and/or on your 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 and hands are free of foreign material before touching your contact lenses, as 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 eye care practitioner.
- Always handle your lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove your 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 your hand rather than between the thumb and fingers.

Lens Wearing Precautions

- CAUTION: Clean and condition lenses prior to use. Lenses come non-sterile.

- 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 nonmovement 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 your 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 cases should be replaced at regular intervals as recommended by the lens case manufacturer or eye care practitioner.

Discuss these topics with your eye care practitioner:

- Wearing of contact lenses during sporting activities.

- Use of any medication in your eyes.

- 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 you not wear contact lenses during work hours.

**CONTRAINDICATIONS (REASONS NOT TO USE)**

DO NOT USE Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy when any of the following conditions exist:

- Acute and subacute inflammations or infection of the anterior segment 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 contact lenses.
- Any active corneal infection (bacterial, fungal or viral).
- If eyes become red or irritated.

**WARNINGS**

Incorrect use of contact lenses and lens care products can result in serious injury to the eye. It is essential for you to follow the eye care practitioner's directions 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 you experience eye discomfort, excessive tearing, vision changes, or redness of the eye, immediately remove the lenses and do not wear them until instructed to do so by the eye care practitioner. You should see your eye care practitioner according to the schedule you were given.

Paragon Z CRT® Contact Lenses for Contact Lens Corneal Refractive Therapy 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 overnight Contact Lens Corneal Refractive Therapy prescribes only overnight wear with removal during the waking hours, and although the safety risks of intermittent overnight wear may not be as great as with sustained overnight wear; there is still increased risk beginning with the first overnight period.

> WARNING
> 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 of the lens 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.

Studies have shown that contact lens wearers who are smokers have a higher incidence of adverse reactions than nonsmokers.

**ADVERSE EFFECTS (PROBLEMS AND WHAT TO DO)**

You should know that the following problems may occur.

- Eyes stinging, burning, itching (irritation), or other eye pain
- 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

If you notice any of these conditions, IMMEDIATELY REMOVE THE LENSES and 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 your eye. Place the lens in the storage case and contact your 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, you should thoroughly clean, rinse and disinfect the lens; then reinsert it.
- If the problem continues, you should IMMEDIATELY remove the contact lenses and consult your eye care practitioner.

When any of the above problems occurs, a serious condition such as infection, corneal ulcer, neovascularization, iritis, persistent stromal edema or GPC (giant papillary conjunctivitis) may be present. 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.

## SUMMARY OF CLINICAL STUDY

### INTRODUCTION

Two hundred four eyes of 102 patients are presented in this report of a study of myopia and myopia astigmatism treatment with overnight wear of contact-lens corneal refractive therapy lenses in tisilfocon A material in a protocol controlled investigation at nine U.S. sites. The objective of this investigation was to determine the safety and effectiveness of the lenses in the population defined in the protocol. The corneal refractive therapy design used in this clinical trial gained FDA market approved on June 13, 2002 when manufactured in paflufocon B and paflufocon D.

### DEMOGRAPHIC INFORMATION

The data presented in this report were collected and analyzed from the 204 eyes of 102 enrolled subjects of which 196 eyes of 98 subjects were treated at nine U.S. centers. The mean age of the full cohort of patients was 34.56 ± 11.6 years (range 11-57). There were 67 female and 31 male subjects enrolled and treated. The data for 72 patients (144 [1] eyes) were analyzed for effectiveness following 6 months of treatment. The mean age of these patients was 34.97± 12.0 years (range 11 to 57). A waiver was granted for one subject that was age 11 years 8 months at the baseline visit. There were 10 adolescent subjects enrolled, 2 withdrew prior to treatment. There were 48 female and 24 male subjects of these 47 were classified Caucasian, 3 were African American, 14 were Asian/Pacific Islander, 1 was American Indian/Aleut Eskimo, and 5 were classified Hispanic.

### EFFECTIVENESS OUTCOMES

The average amount of myopia (nearsightedness) that can be expected to be corrected is shown in Table 1. These values assessed on 137 eyes on which full correction was attempted are only averages and some patients can be expected to achieve more or less than these averages. Seven patients were given a monovision treatment. Monovision is an alternative method when bifocal correction is required where one eye is corrected for distance vision and the other eye is corrected for reading.

[1] At 1 month one subject converted to, and completed wearing only one lens.

Table 1

AVERAGE REDUCTION IN MYOPIA (DIOPTERS) N=137*

| Refractive Range and Count | Average Subjective Refraction (MRSE) | Average Myopia Reduction (MRSE) | Average Residual Subjective Refraction (MRSE) |
|---|---|---|---|
| -0.25>-1.00 N=8 | -0.89 | 0.81+/ -0.48 | -0.08+/ -0.38 |
| -1.25>-2.00 N=40 | -1.63 | 1.49+/ -0.45 | -0.13+/ -0.40 |
| -2.25>-3.00 N=46 | -2.57 | 2.37+/ -0.62 | -0.20+/ -0.57 |
| -3.25>-4.00 N=25 | -3.67 | 3.23+/ -0.67 | -0.44+/ -0.62 |
| -4.25>-5.00 N=13 | -4.40 | 3.88+/ -0.67 | -0.52+/ -0.60 |
| -5.25>-6.00 N=5 | -5.50 | 5.65+/ -0.55 | 0.15+/ -0.55 |

*All completed eyes targeted for emmetropia.

Uncorrected Visual Acuity (UCVA)

Post treatment visual acuity was assessed on 137 eyes on whom full correction was attempted. Of these eyes 41.5% obtained 20/20 or better uncorrected visual acuity and 94.8% obtained 20/40 or better visual acuity at 6 months. See the following table.

Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy provided a temporary full reduction in some patients with up to -5.5 diopters of myopia. For patients with greater than -5.5 diopters of myopia only a partial reduction of myopia can be expected. The percentage of patients that can be expected to achieve full or partial temporary refractive reduction based on 144 [2] treated eyes is shown in Table 2.

Table 2

PERCENT OF COMPLETED EYES THAT ACHIEVED FULL OR PARTIAL TEMPORARY REDUCTION OF MYOPIA

| INITIAL MYOPIA | FULL REDUCTION ± 0.50 D from Target* | PARTIAL REDUCTION ± 1.00 D from Target* | FINAL V.A. 20/20 or better** | FINAL V.A. 20/40 or better** |
|---|---|---|---|---|
| 1.00 D or less | 88% | N/A | 50% | 100% |
| -1.25 to - 2.00 D | 83% | 100% | 60% | 95% |
| -2.25 to - 3.00 D | 81% | 95% | 39% | 93% |
| -3.25 to - 4.00 D | 70% | 93% | 24% | 92% |
| -4.25 to - 5.00 D | 79% | 86% | 23% | 100% |
| -5.25 to -6.00 D | 33% | 83% | 33% | 100% |

* N=144 for reduction (all efficacy qualified eyes)

** N=137 for Final VA (only eyes targeted for emmetropia)

[2] At 1 month one subject converted to, and completed wearing only one lens.

Accuracy

Accuracy of outcome was evaluated by analysis of attempted versus achieved manifest refraction spherical equivalent. At the 6 month visit, 77.6% (111/144 [3]) of 6 month completed eyes were within 0.50 D attempted spherical equivalent correction, and 95.1% (136/144) of eyes were within 1.00 D of attempted correction. In this clinical study the higher the initial myopia the lower the percentage of patients achieved full correction and/or 20/20 vision. The preceding table demonstrates the relationship of initial myopia with treatment success.

There is reference in a published study [4] regarding visual acuity in the "better seeing eye" of a subject as a useful method of estimating functional vision when using both eyes. Of course, very few patients need to rely on the vision from a single eye. When the study subjects were analyzed for only their "better seeing eye", 86% had 20/20 or better vision, and 100% had 20/40 or better. The accuracy calculation also changes slightly. 80% Are estimated to be within 0.5 D of target; 96% are estimated to be within 1.0 D of target in keeping with the method of better eye analysis.

Wearing Time

The lenses were used for overnight wear only. They were applied within 30 minutes of sleep and removed within 30 minutes of awakening. The average wearing time was 6 to 8 hours and reflected the expected distribution of night-sleep time. There was no apparent relationship between the number of hours of wear during sleep and the visual acuity outcome for any amount of pretreatment myopia.

REGRESSION OF VISUAL ACUITY

To help you assess the change over time following lens removal, subjects in the clinical study were evaluated at 8, 24, 48, and 72 hours after removal of their lenses following either the six or nine month scheduled visit. Remember that the times given are averages, many patients will do better, many will not fare as well. The 1 Diopter regression point was chosen because it approximately corresponds to 20/40 unaided vision, the legal requirement for driving in many states.

The following guidance Table 3 is intended for counseling patients regarding the stability of their vision throughout the day. Values in the table represent the number of hours from the time of lens removal before the average patient's vision will have regressed to the point that his refraction is -1.0 Diopter (roughly corresponding to 20/40).

To use the chart, find your original pretreatment manifest refractive spherical equivalent (MSRE) in the 3rd horizontal row then move down that column to the row where the refraction (in column 2) matches the refraction you achieved immediately on lens removal after a night's wear. The bold value found in the cell identified in this way represents the average number of hours that similar patients have experienced before their refractive error has regressed to approximately -1.0 Diopter. Beneath that value is the minimum projected time for any subject in the study. This is only a guideline; every patient should test his/her vision as it relates to the requirements of their own daily schedules.

[3] At 1 month one subject converted to, and completed wearing only one lens.

[4] Monocular Versus Binocular Visual Acuity as Measures of Vision Impairment and Predictors of Visual Disability, Rubin, et al, Invest Ophthalmol Vis Sci 2000; 41:3327-3334

Table 3

AVERAGE AND MINIMUM HOURS UNTIL REGRESSION TO -1.0 DIOPTER OR WORSE

**(estimated for all subjects with pretreatment MRSE > -1.0 D targeted for emmetropia and corrected to better than -1.0 D MRSE N=79)**

| REFRACTION AT LENS REMOVAL | | | -1.12 to -2.00 | -2.12 to -3.00 | -3.12 to -4.00 | -4.12 to -5.00 | -5.12 to -6.00 |
|---|---|---|---|---|---|---|---|
| | +0.50 | **Mean** | **163.7 Hrs** | **52.6 Hrs** | **19.8 Hrs** | **12.1 Hrs** | **16.9 Hrs** |
| | | Minimum | 9.3 Hrs | 3.7 Hrs | 4.3 Hrs | 5.3 Hrs | 5.5 Hrs |
| | +0.25 | **Mean** | **162.3 Hrs** | **51.6 Hrs** | **18.9 Hrs** | **11.4 Hrs** | **15.9 Hrs** |
| | | Minimum | 9.3 Hrs | 3.5 Hrs | 4.1 Hrs | 4.9 Hrs | 5.1 Hrs |
| | 0.00 | **Mean** | **159.4 Hrs** | **49.9 Hrs** | **17.5 Hrs** | **10.5 Hrs** | **14.4 Hrs** |
| | | Minimum | 9.2 Hrs | 3.2 Hrs | 3.9 Hrs | 4.4 Hrs | 4.7 Hrs |
| | -0.25 | **Mean** | **153.5 Hrs** | **46.9 Hrs** | **15.5 Hrs** | **9.1 Hrs** | **12.3 Hrs** |
| | | Minimum | 9.1 Hrs | 2.8 Hrs | 3.4 Hrs | 3.8 Hrs | 4.1 Hrs |
| | -0.50 | **Mean** | **139.7 Hrs** | **41.1 Hrs** | **12.3 Hrs** | **7.1 Hrs** | **9.5 Hrs** |
| | | Minimum | 8.5 Hrs | 2.2 Hrs | 2.8 Hrs | 2.9 Hrs | 3.1 Hrs |
| | -0.75 | **Mean** | **103.9 Hrs** | **28.8 Hrs** | **7.5 Hrs** | **4.3 Hrs** | **5.5 Hrs** |
| | | Minimum | 5.1 Hrs | 1.2 Hrs | 1.6 Hrs | 1.6 Hrs | 1.8 Hrs |

Effects On Astigmatism

Corneal Refractive Therapy does not predictably affect the magnitude of pretreatment astigmatism. Either increases or decreases in astigmatism may occur following Contact Lens Corneal Refractive Therapy. Of the eyes that completed the nine-month clinical study, 27% showed no change in refractive astigmatism, 49% showed a decrease of one diopter or less and 1% showed a decrease more than one diopter, while 23% showed an increase of one diopter or less and 1% showed an increase greater than one diopter of refractive astigmatism.

## OVERNIGHT WEAR SAFETY SUMMARY

In this trial, 196 eyes from 98 patients were evaluated for safety during six months overnight wear corneal refractive therapy when treating myopia and myopia with astigmatism. These data are a reliable indicator of the safety of these lenses in an overnight corneal refractive therapy modality. In this study analysis of safety outcomes was performed for BSCVA losses, adverse events, complications, intraocular pressure, slit lamp findings and symptoms problems and complaints. The analysis was completed for all eyes that reported at all visits.

Best Spectacle-Corrected Visual Acuity (BSCVA)

After passing the dispensing and a successful day one visit, of the 204 eyes originally enrolled in the study, 35 were found, at one point or another, to have temporarily lost 2 lines of BSCVA from baseline. Additionally, eight subjects were observed to temporarily have BSCVA's of 20/40 or worse.

Five completed eyes, 3.5% (5/144) manifested a transient loss of two or more lines of BSCVA at the six month visit. All losses except one were found to be transient as they were not found to be present at the post-removal visits. In one case recovery was not documented before the eye was lost to follow-up. There were no eyes with BSCVA worse than 20/40 at the six month visit.

Although the range of durations until documented recovery was 0 to 216 days (one subject could not be returned for documentation), the median duration was 18 days. Of the 15 occurrences beyond the early fitting period none were bilateral and none worse than 20/32 in that eye. Only two of these eyes demonstrated visual acuities worse than 20/40 when first observed and they were documented to have been resolved at their next follow-up visit in 7 and 21 day respectively.

Absence of Persistent Corneal Change

The protocol stipulates that all treated eyes of subjects who discontinued the clinical trial must be followed one month post discontinuation and every one month thereafter until there was no difference greater than 0.50 D in either of the keratometric meridians from the baseline measures. Of 58 discontinued eyes of the 29 discontinued subjects, 39 eyes of 20 subjects were within 0.50 D of the baseline measurements at the discontinuation visit. One of the discontinued subjects (2 eyes) was lost to follow-up during the investigation. Eleven eyes of 6 subjects were measured to be within 0.50 D of their baseline visit at a post discontinuation visit. Two enrolled subjects were not dispensed.

Symptoms, Complaints and Discontinuations

Of the 98 subjects who had at least one night of treatment, 29 were discontinued prior to the six month visit. Table 4 below reports the tabulation of all 102 subjects that were discontinued prior to the six month visit and the reason for discontinuation.

**Table 4**

**Reason for Discontinuation**
**(N=102)**

| Reason for Discontinuation | Number of Patients |
|---|---|
| Unacceptable Visual Acuity | 13 |
| Other | 6 |
| Lack of Comfort | 3 |
| Lack of Interest | 5 |
| Protocol Violation | 2 |
| Missed Visits | 0 |
| Pathology | 0 |

The reasons given for "other" include two subjects who reported lens adherence and one that reported "lens slipping" at night, one who had back surgery and could not attend visits, and two not dispensed. The protocol violation listing includes two subjects who stopped wear of the lenses for long periods during the study.

The clinical reasons for discontinuation are unacceptable vision, lack of comfort, lens adherence and lens slipping that account for 13 % (13/98), 3 % (3/98), 2% (2/98) and 1% (1/98) respectively. The total discontinuation rate for clinical reasons was 19 %.

Table 5 lists complaints and symptoms reported at doctor visits.

**Table 5**

PERCENT OF EYES EXHIBITING COMPLAINT OR SYMPTOM AT VISIT

| Visit | Unscheduled | 2-Week | 1-Month | 2-Month | 3-Month | 6-Month |
|---|---|---|---|---|---|---|
| Total Eyes at Visit | 260 | 168 | 156 | 164 | 160 | 144 |
| None | 39% | 44% | 63% | 68% | 69% | 81% |
| Discomfort | 24% | 20% | 15% | 14% | 15% | 8% |
| Itching/Burning | 6% | 4% | 0% | 4% | 1% | 0% |
| Blurred Vision | 26% | 20% | 8% | 4% | 4% | 5% |
| Dryness/Scratch | 6% | 3% | 6% | 7% | 3% | 5% |
| Redness | 5% | 2% | 1% | 0% | 0% | 0% |
| Variable Vision | 12% | 15% | 4% | 2% | 4% | 3% |
| Photophobia | 3% | 1% | 0% | 0% | 1% | 0% |
| Halos | 4% | 11% | 8% | 5% | 3% | 1% |
| Ghost Images | 0% | 1% | 1% | 1% | 0% | 1% |
| Lens Adhesion | 5% | 2% | 1% | 0% | 1% | 1% |
| Lens Need Cleaning | 2% | 5% | 1% | 3% | 0% | 1% |
| Other | 6% | 3% | 1% | 1% | 0% | 2% |

Adverse Events and Complications

The following is the description of the adverse events discussed in the report: Subject 904 – peripheral corneal infiltrate – discontinued lens wear – administered medication - resolved in 7 days; Subject 1002 – two incidents of corneal infiltrates – discontinued lens wear – administered medication – each occurrence resolved in 6 days.

There were twenty-one positive reports of lens adherence in thirteen eyes of nine subjects. Only one of these eyes had lens adherence at multiple visits.

Patient Satisfaction

Fifty-nine of the 72 completed subjects (85.3%) rated their overall satisfaction with their unaided vision equivalent to very good or excellent at the 6-month visit compared to no subjects (0.0%) for the same equivalent rating pre treatment.

## MAINTAINING EFFECTS OF PARAGON Z CRT® LENSES FOR CORNEAL REFRACTIVE THERAPY

The long-term wear of Paragon Z CRT® Contact Lenses for Corneal Refractive Therapy does not eliminate the need to continue wearing contact lenses to produce the reduction in myopia. After the cornea has been changed by wearing these contact lenses, you must continue overnight wear of lenses to maintain the results. Usually the treatment lenses will continue to be the lenses worn after successful treatment. In unusual circumstances, new lenses may be prescribed that are Myopic Reduction Maintenance Lenses or Retainer Lenses. Such Retainer Lenses would be only a slight modification of the patient's Paragon Z CRT® prescription.

The wearing schedule for Paragon Z CRT® contact lenses or Retainer Lenses may vary from the schedule prescribed during treatment. In cases of low pretreatment myopia, the effect may last for more than one day.

Note: To maintain the Contact Lens Corneal Refractive Therapy 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.

## GLOSSARY

| | |
|---|---|
| Adnexa | Tissues near to the eye |
| Adverse Effects | Undesirable effects |
| Aphakia | Eye that does not have a lens structure |
| Astigmatism | Eye condition in which one or more surfaces of the cornea or lens has a shape that is not round but more like that of a spoon |
| Best Spectacle Corrected Visual Acuity (BSCVA) | Best vision you can achieve wearing glasses in your exact prescription under optimum viewing conditions |
| Biomicroscope | An instrument that uses magnification to examine the eye |
| Contact Lens Corneal Refractive Therapy (CRT) | Contact lens fitting procedure that results in a reduction of nearsightedness while lenses are worn and for a temporary period after the contact lenses have been removed (typically 1 day if worn overnight) |
| Contact Lens Sticking | Lack of movement of a contact lens on the cornea |
| Cornea | The clear, bubble-like structure on the front of the eye, where light first enters the eye |
| Corneal Edema | Accumulation of fluid in the cornea resulting in swelling |
| Corneal Hypoesthesia | Partial loss of sensitivity to touch in the cornea |
| Corneal Staining | Bright areas on the cornea where dye collects and which indicates an abrasion or other disturbance of the cornea |
| Corneal Ulcer | Small area of tissue loss in the cornea |
| Disinfection | Destruction of bacteria and viruses but not some spores |
| Diopter | Unit of power for glasses or contact lenses |
| Enzyming Contact Lenses | Placing contact lenses in a solution that contains an enzyme that dissolves proteins on the surface of the lens |
| Giant Papillary Conjunctivitis | Allergic type of conjunctival inflammation on the under surface of the upper eyelid. |
| Iritis | Infection of the iris or colored portion of the eye |
| Lacrimal Secretion | Tearing |
| Manifest Refraction Spherical Equivalent | A measure of vision correction requirements (in diopters), which combines your myopia and your astigmatism |
| Myopia | Nearsightedness, inability to see distant objects clearly |

| | |
|---|---|
| Myopic Reduction Maintenance Lens | A modification of the Corneal Refractive Therapy contact lens design in which the central portion of the lens applies just enough pressure to the cornea to maintain the corneal flattening achieved but with no additional corneal flattening. Such a lens is usually not needed with the Paragon Z CRT® and Paragon CRT® 100 design since the treatment lens performs this function. |
| Neovascularization | New blood vessel growth in the cornea |
| Orthokeratology | Predecessor to Contact Lens Corneal Refractive Therapy using a series of lenses to achieve a temporary reduction in myopia |
| Refract | Bending of light in order to make it focus |
| Refractive Anomalies | Eye conditions leading to blurred vision including nearsightedness, farsightedness and astigmatism |
| Retainer Lens | Another name for the Myopic Reduction Maintenance Lens |
| Retina | Structure at the back of the eye that receives the light image |
| Rewetting Contact Lenses | Placing a solution in the eye while contact lenses are worn that acts as an artificial tear to wet the lens |
| Sticking Lens | Lens on the cornea that does not move |
| Stromal edema | Swelling of the cornea |
| Ulcerative keratitis | Damage to the cornea usually caused by a bacterial, fungal or viral infection |

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