

PACKAGE INSERT

IMPORTANT - Please read carefully and keep this information for future use. This package insert is intended for the eyecare professional, but should be made available to patients upon request. The eyecare professional should provide the patient with the patient instructions that pertain to the patient's prescribed lens.

CAUTION: Federal (U.S.A) law restricts this device to sale by or on the order of a licensed eyecare professional.

Menicon Z™ (tisilfocon A)

Rigid Gas Permeable Contact Lenses

Spherical and Aspheric Lenses for Myopia and Hyperopia
Toric Lenses to Correct Astigmatism
Multifocal Lenses for Presbyopia
in Aphakic and Non-Aphakic Persons

DESCRIPTION:

The Menicon Z™ (tisilfocon A) Rigid Gas Permeable Contact Lens is available as a daily wear spherical, aspheric, prism ballast toric or multifocal design and as an extended wear lens for up to 30 days/29 nights in spherical, aspheric, non-prism ballast toric and multifocal designs.

The lens material (tisilfocon A) is a thermoset copolymer derived from fluoro-methacrylate and siloxanystyrene, bound by crosslinking agents. The lens is available in a light blue tint. The blue lens is tinted with color additive D & C Green No. 6. Also, a UV absorber (Benzotriazol) is added as an additive during the manufacturing process.

The Menicon Z™ (tisilfocon A) Contact Lens is a hemispherical shell of the following dimensions (not all parameter combinations are available in all designs):

Spherical and Aspheric Lens:

Diameter	7.0 to 12.0mm
Center Thickness	0.08 to 0.50mm (daily wear) 0.08 to 0.38mm (extended wear)
Base Curve	6.50 to 9.00mm
Powers	-25.00 to +25.00D (in 0.25D steps) (daily wear) -25.00 to +8.00D (in 0.25D steps) (extended wear)

Toric lens:

Diameter	7.0 to 11.0mm
Center Thickness	0.08 to 0.50mm (daily wear) 0.08 to 0.38mm (extended wear)
Base Curve	7.30 to 8.50mm
Sphere Powers	-10.00 to +8.00D (in 0.25D steps)
Cylinder Powers	-0.50 to -5.00D (in 0.25D steps)
Prism Ballast	0.75 to 2.00D (in 0.25D steps) (daily wear only)
Truncation Height	0.0 to 1.0mm (in 0.1mm steps) (daily wear only)

Multifocal Lens (Centered, Decentered, Crescent):

Diameter	8.8 to 11.0mm
Center Thickness	0.08 to 0.65mm (daily wear) 0.08 to 0.38mm (extended wear)
Base Curve	7.00 to 9.00mm
Sphere Power	-13.00 to +5.00D
Add Power	+1.00 to +3.00D

The physical/optical properties of the lens are:

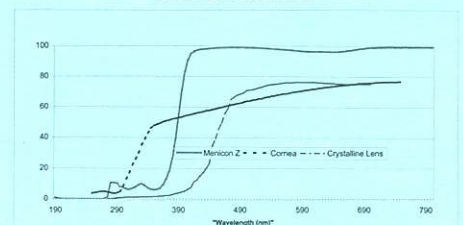
Specific Gravity:	1.20
Refractive Index:	$n_D^{25} 1.436 \pm 0.001$
Surface Character:	Hydrophobic
Wetting Angle:	24 degrees (after soaking)
Light Transmittance:	Visible region >95% (380 nm – 780 nm) Ultraviolet region <6% (210 nm – 380 nm) (sample thickness 0.08mm)
Water Absorption:	Less than 0.5% by weight
Oxygen Permeability:	$163 \times 10^{-11} \text{ (cm}^2/\text{sec)(mL O}_2\text{/(mL x mmHg)) Dk}^*$ $189 \times 10^{-11} \text{ **}$ $250 \times 10^{-11} \text{ ***}$

* Method for determination of oxygen permeability: ISO/DIS 9913.1 1994. Optics and optical instruments - Contact lenses - Part 1: Determination of oxygen permeability and transmissibility with the Fatt method. (PHEMA Standard)

** Measurement of Dk by Fatt, Polarographic method. (PHEMA Standard)

*** Measurement of Dk by the Hamano Polarographic method. (Teflon Standard)

WAVELENGTH nm



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., Hitchens, V.M., *Optical Radiation and Visual Health*, CRC Press, Boca Raton, Florida, 1986, p. 19, figure 5.

Note: Long-term exposure to UV radiation is one of the risk factors associated with cataracts. Exposure is based on a number of factors such as environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV-absorbing contact lenses help provide protection against harmful UV radiation. However, clinical studies have not been done to demonstrate that wearing UV-absorbing contact lenses reduces the risk of developing cataracts or other eye disorders. Consult the eyecare professional for more information.

ACTIONS

The Menicon Z™ (tisilfocon A) Contact Lens, when placed on the cornea, acts as a refracting medium to focus light rays on the retina.

The Menicon Z™ (tisilfocon A) Contact Lens is a lathe cut firm contact lens with spherical or aspheric back surfaces. The posterior curve is selected to properly fit an individual eye, and the anterior curve is selected to provide the necessary optical power to correct refractive error. A peripheral curve system on the posterior surface allows tear exchange between the lens and the cornea.

The Menicon Z™ (tisilfocon A) Toric Contact Lens provides a more even surface over the different curvatures of the astigmatic cornea and thus helps to focus light rays on the retina.

The Menicon Z™ (tisilfocon A) Multifocal Contact Lens provides the necessary optical powers to correct different refractive errors for distance and near requirements.

INDICATIONS (USES):

Menicon Z™ (tisilfocon A) spherical, aspheric, prism ballast toric and prism ballast multifocal lenses are indicated for daily wear for the correction of refractive error (myopia, hyperopia, presbyopia and/or astigmatism) in aphakic and non-aphakic persons with non-diseased eyes.

Menicon Z™ (tisilfocon A) spherical, aspheric, non-prism ballast toric and non-prism ballast multifocal lenses are indicated for extended wear (from 1 to 30 days between removals for cleaning and disinfection of the lenses, as recommended by the eyecare professional) for the correction of refractive error (myopia, hyperopia, presbyopia and/or astigmatism) in non-aphakic persons with non-diseased eyes.

The lens may be prescribed in spherical and aspheric powers ranging from -25.00 D to +25.00 D for daily wear and -25.00 D to +8.00 D for up to 30 days extended wear. Toric lenses are designed to correct up to 5.00 D of astigmatism and multifocal lenses to provide up to +3.00 D of reading add power for up to 30 days extended wear.

The lens may be disinfected using a chemical disinfection system only.

See **WARNINGS** for information about the relationship between wearing schedule and corneal complications.

CONTRAINDICATIONS (REASONS NOT TO USE):

DO NOT USE the Menicon Z™ (tisilfocon A) Contact Lens when any of the following conditions exist:

- Acute and subacute inflammation 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 lacrimal secretion (dry eyes)
- Corneal hypoesthesia (reduced corneal sensitivity)
- Any systemic disease that may affect the eye or be exaggerated by wearing contact lenses
- Allergic reactions of ocular surfaces or surrounding tissues that 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 the Menicon Z™ (tisilfocon A) Contact Lens
- Any active corneal infection (bacterial, fungal, or viral)
- If eyes become red or irritated
- Incomplete healing following eye surgery

WARNINGS:

Patients should be advised of the following warnings pertaining to contact lens wear:

- Problems with contact lenses and lens care products could result in **serious injury** to the eye. It is essential that patients follow their eyecare professional's direction and all labeling instructions for proper use of lenses and lens care products, including the lens case. Eye problems, including corneal ulcers, can develop rapidly and lead to **loss of vision**.
- Daily wear lenses are not indicated for overnight wear, and patients should be instructed not to wear lenses while sleeping. Clinical studies have shown that the risk of serious adverse reactions is increased when these lenses are worn overnight.
- Smoking increases the risk of corneal ulcers for contact lens users, especially when lenses are worn overnight or while sleeping.^{1,2}
- The risk of ulcerative keratitis has been shown to be greater among users of extended wear lenses than among users of daily wear lenses. The risk among extended wear lens users 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 case. The long-term risk of microbial keratitis has not been determined for this lens when worn for greater than 7 days extended wear. Postmarketing studies are in progress to evaluate the risk up to 30 days.
- If a patient experiences **eye discomfort**, excessive tearing, vision changes, or redness of the eye, the patient should be instructed to **immediately remove lenses** and promptly contact his or her eyecare professional.
- **UV-absorbing contact lenses are NOT substitutes for protective UV-absorbing eyewear such as UV-absorbing goggles or sunglasses because they do not completely cover the eye and surrounding area. Persons should continue to use their protective UV-absorbing eyewear as directed.**

¹CLAO Journal, January 1996; Volume 22, Number 1, pp. 30-37

²New England Journal of Medicine, September 21, 1989; 321 (12), pp. 773-783

PRECAUTIONS:

CAUTION: NON-STERILE. ALWAYS CLEAN AND DISINFECT LENSES PRIOR TO USE.

Special Precautions for Eyecare Professionals:

- Due to the small number of patients enrolled in clinical investigation of lenses, all refractive powers, design configurations, or lens parameters available in the lens material are not evaluated in significant numbers. Consequently, when selecting an appropriate lens and wear schedule for a patient, the eye care professional should consider all lens characteristics that can affect lens performance and ocular health, including oxygen permeability, wettability, central and peripheral thickness, and optic zone diameter.

Lens designs with an average thickness over the central 6 mm greater than 0.19 mm (Rx outside the range of -0.25 to -15.00 in thin lens designs) do not provide oxygen transmissibility above the established threshold level required to prevent overnight corneal edema³. Thin lens

Lenses should be removed daily for cleaning and disinfecting (according to lens care system instructions) before wearing.

Extended Wear (Overnight)*

- **Lens Designs Approved for extended wear range from +8.00 to -25.00D. Prism ballast designs are not approved for extended wear.**
 - **It is suggested that new contact lens wearers first be evaluated on a daily wear schedule. If the patient is judged to be an acceptable extended wear candidate, the eyecare professional may determine an extended wear schedule based upon the response of the patient.**
 - The eyecare professional should establish an extended wear period up to a maximum of 30 continuous days/29 nights that is appropriate for each patient. Once the lenses are removed, the patient's eyes should have a rest period with no lens wear of overnight or longer, as recommended by the eyecare professional.
 - See **WARNINGS** for information about the relationship between wearing schedule and corneal complications and **CLINICAL RESULTS** for important information about average wear times and other study findings.
- * If the lenses continue to be well tolerated.

LENS CARE DIRECTIONS:

Note: ABRASIVE SURFACTANT CLEANERS SUCH AS BOSTON®, BOSTON ADVANCE®, OPTI-FREE® AND OPTI-SOAK® SHOULD NOT BE USED. Eyecare professionals should review with the patient lens care directions, including both basic lens care information and specific instructions on the lens care regimen recommended for the patient:

General Lens Care

Basic Instructions:

- Always wash and rinse hands before handling contact lenses.
- Always use **fresh unexpired** lens care solutions.
- Use the recommended chemical (not heat) system of lens care. Carefully follow instructions on solution labeling. Different solutions cannot always be used together, and not all solutions are safe for use with all lenses. **Do not alternate or mix lens care systems unless indicated on solution labeling.**
- Do not use saliva or anything other than the recommended solutions for lubricating or rewetting lenses. Do not put lenses in the mouth.
- Lenses should be **cleaned, rinsed, and disinfected** each time they are removed. **Cleaning and rinsing** are necessary to remove mucus and film from the lens surface. **Disinfecting** is necessary to destroy harmful germs.
- Always remove, clean, rinse, enzyme (as recommended by the eyecare professional) and disinfect lenses according to the schedule prescribed by the eyecare professional. The use of an enzyme or any cleaning solution **does not substitute for disinfection.**
- The lens care products listed below are recommended by Menicon for use with the Menicon Z™ (tisilfocon A) Contact Lens. See Package Insert for other products that may be used with this lens. Eyecare professionals may recommend alternate solutions that are appropriate for the patient's use with his or her lens. Care should be taken not to mix solutions from different companies and/or care systems unless specifically instructed to do so by the eye care professional.

RECOMMENDED CARE SYSTEM:

LENS CARE TABLE

Solution Purpose	Claris® Gas Perm Care System Chemical (not heat) disinfection
Cleaning	Claris® Cleaning and Soaking Solution
Rinsing	Lens Plus® Sterile Saline Solution or other solution as recommended by your eye care professional
Disinfection/Storage	Claris® Cleaning and Soaking Solution
Lubrication/Rewetting	Claris® Rewetting Drops
Periodic Protein Cleaning	ProFree/GP Weekly Enzymatic Cleaner

Claris® and Lens Plus® are trademarks of AMO, Inc.

ALTERNATE CARE SYSTEMS:

LENS CARE TABLE

Solution Purpose	Optimum by Lobob® Chemical (not heat) disinfection
Cleaning	Optimum by Lobob® Cleaning, Disinfecting and Storage Solution
Rinsing	Rinsing solution as recommended by eye care professional
Disinfection/Storage	Optimum by Lobob® Cleaning, Disinfecting and Storage Solution
Lubrication/Rewetting	Optimum by Lobob® Wetting/Rewetting Drop and In-the-eye Lubricant
Periodic Cleaner	Optimum by Lobob® Extra Strength Cleaner

Optimum by Lobob® is a trademark of Lobob® Laboratories, Inc.

- Note: Some solutions may have more than one function, which will be indicated on the label. Read the label on the solution bottle, and follow instructions.
- Clean one lens first (always the same lens first to avoid mix-ups) with a recommended cleaning solution. Rinse the lens thoroughly with recommended solution to remove the cleaning solution, mucus, and film from the lens surface, and put that lens into the correct chamber of the lens storage case. Then repeat the procedure for the second lens.
- After cleaning, disinfect lenses using the system recommended by the manufacturer and/or the eyecare professional.
- To store lenses, disinfect and leave them in the closed/unopened case until ready to wear. If lenses are not to be used immediately following disinfection, the patient should be instructed to consult the package insert or the eyecare professional for information on storage of lenses.
- After removing the lenses from the lens case, empty and rinse the lens storage case with solution as recommended by the lens case manufacturer; then allow the lens case to air dry. When the case is used again, refill it with storage solution. Replace lens case at regular intervals as recommended by the lens case manufacturer or your eyecare professional.

- Eyecare professionals may recommend a **lubricating/rewetting** solution, which can be used to wet (lubricate) lenses while they are being worn to make them more comfortable.
- Menicon Z™ (tisilfocon A) Contact Lenses **cannot** be heat (thermally) disinfected.

Chemical (Not Heat) Disinfection:

- Clean the contact lenses with a recommended cleaning solution and thoroughly rinse them with a recommended rinsing solution.
- After cleaning, to disinfect, carefully follow the instructions accompanying the disinfecting solution in the care regimen recommended by the lens manufacturer or the eyecare professional.
- Thoroughly rinse lenses with a fresh saline solution recommended for rinsing before inserting and wearing, or follow the instructions on the disinfection solution labeling.
- Do not heat the disinfection solution and lenses.
- Leave the lenses in the unopened storage case until ready to put on the eyes.
- **Caution:** Lenses that are chemically disinfected may absorb ingredients from the disinfecting solution which may be irritating to the eyes. A thorough rinse in fresh sterile saline solution (or follow the instructions on the disinfection solution labeling) prior to placement on the eye should reduce the potential for irritation.

LENS DEPOSITS AND USE OF ENZYMATIC CLEANING PROCEDURE:

Enzyme cleaning may be recommended by the eyecare professional. Enzyme cleaning removes protein deposits on the lens. These deposits cannot be removed with regular cleaners. Removing protein deposits is important for the well-being of the patient's lenses and eyes. If these deposits are not removed, they can damage the lenses and cause irritation. For extended wear patients in particular, enzymatic cleaning is recommended each time the lenses are removed for an overnight break. Daily wear patients have also been shown to benefit from periodic enzymatic cleaning. Your eyecare professional will recommend a schedule that is right for you.

Enzyme cleaning does NOT replace routine cleaning and disinfecting. For enzyme cleaning, the patient should carefully follow the instructions in the enzymatic cleaning labeling.

CARE FOR A STICKING (NON-MOVING) LENS:

If the lens sticks (stops moving), the patient should be instructed to apply a few drops of the recommended lubricating or rewetting solution directly to the eye and wait until the lens begins to move freely on the eye before removing it. If nonmovement of the lens continues after 10 minutes, the patient should **immediately** consult the eyecare professional.

EMERGENCIES:

The patient should be informed that 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. CONTACT THE EYECARE PROFESSIONAL OR VISIT A HOSPITAL EMERGENCY ROOM WITHOUT DELAY.

HOW SUPPLIED:

Each Menicon Z™ (tisilfocon A) Contact lens is shipped non-sterile immersed in Alcon® Unique-pH™ Multi-Purpose Solution (0.0011% polyquaternium-1 and 0.01% edetate disodium as preservatives) in an individual plastic container. If the patient is sensitive to edetate disodium or polyquaternium-1, the lens should be removed from the plastic container upon receipt, rinsed with fresh saline solution, cleaned with a cleaner and placed in another prescribed disinfecting solution prior to dispensing. Follow the manufacturer's instructions on the disinfecting solution label.

Dry shipped lenses are available upon request.

The plastic container, packing slip or invoice is marked with the information for base curve, diopter power, diameter, center thickness, color, UV-absorber, lot number, hydration date and other required parameters specified by the design.

REPORTING OF ADVERSE REACTIONS:

All serious adverse experiences and adverse reactions observed in patients wearing Menicon Z™ (tisilfocon A) Contact Lenses should be reported to:

Menicon America, Inc.
1840 Gateway Drive
San Mateo, CA 94404
1-800-MENICON(1-800-636-4266)

Menicon Z™

05/2004 LMS0019-01

Control cohort. The events are shown by type in the following table (the columns headed "Subjects" present the number of subjects with a specific Adverse Event as a proportion of the total subjects in each cohort).

Adverse Events by Type All Test and Control Subjects		
CORNEAL ADVERSE EVENTS	Subjects	
Inflammatory/Infectious Events	Test	Control
Infiltrative Keratitis	0.3%	2.6%
Vascularized Limbal Keratitis	0.6%	0.0%
Corneal Ulcers	0.3%	0.3%
Abrasions		
Foreign Body	2.8%	0.3%
Metabolic	0.0%	0.3%
Unknown	0.0%	0.6%
Chemical	0.3%	0.3%
Edema		
Microcystic	0.0%	0.3%
CONJUNCTIVAL ADVERSE EVENTS		
Bacterial	0.6%	2.9%
Viral	0.3%	0.0%
Allergic	1.3%	0.6%
GPC	0.3%	0.6%
Unknown	0.3%	0.6%
MISCELLANEOUS ADVERSE EVENTS		
Sinus Infection	0.0%	0.3%
Trauma	0.0%	0.3%
Lens Displacement	0.0%	0.3%
Neurological	0.0%	0.3%
Episcleritis	0.3%	0.3%
Lacrimal Occlusion	0.3%	0.0%
Lens Awareness	0.3%	0.0%
Total Subjects	317	313

There were 18 reports of lens adherence for the Test group. These 18 reports were for 10 subjects/16 eyes.

Discontinued Subjects

There were 59 Test subjects and 103 Control subjects discontinued during the 12 month clinical. The reasons for discontinuation were as follows:

Reasons for Discontinuation By Cohort

	Test Subjects	Control Subjects
Subjects Enrolled	317	313
Lost to Follow-up	3.8%	9.3%
Protocol Violation	2.8%	6.7%
Comfort	3.8%	5.1%
Subject Decision	4.1%	3.5%
Positive Slit Lamp Findings:		
Related to Study Len	0.9%	2.6%
Unrelated to Study Lens	0.0%	0.3%
Adverse Event	0.9%	2.2%
Investigator Decision	1.3%	1.3%
Unacceptable Visual Acuity	0.0%	0.3%
Other:	0.9%	1.6%

There were 3 Test subjects and 9 Control subjects discontinued for

Positive Slit Lamp Findings. The 3 Test subjects were discontinued for epithelial hypertrophy at 389 o'clock, increased neovascularization, and limbal desiccation. The 9 Control subjects discontinued for Positive Slit Lamp Findings were discontinued for neovascularization, microcysts/edema, GPC, and infiltrates.

There were 3 Test subjects and 7 Control subjects discontinued for Adverse Event. The 3 Test subjects were discontinued for epithelial corneal defect, allergic reaction, and marginal ulcerative keratitis. The 7 Control subjects were discontinued for microcystic edema, multiple incidents of keratitis, acute ocular inflammation, sector field defect, corneal ulcer, and infiltrative keratitis.

FITTING:

Conventional methods of fitting contact lenses apply to Menicon Z™ (tisilfocon A) Contact Lenses. For a detailed description of the fitting techniques, refer to the Menicon Z™ (tisilfocon A) Professional Fitting and Information Guide, copies of which are available from:

Menicon America, Inc.
1840 Gateway Drive
San Mateo, CA 94404
1-800-MENICON(1-800-636-4266)

WEARING SCHEDULE:

The wearing schedule should be determined by the eyecare professional. Not all patients can achieve the maximum wear time of up to 30 days of continuous wear. Patients should be monitored closely during the first month of 30-day continuous wear. **If problems occur during this first month, the patient may not be suitable for the full 30-day wearing schedule.** The maximum suggested wearing time should be determined by the eyecare professional based upon the patient's physiological eye condition because individual responses to contact lenses vary. Regular check-ups, as determined by the eyecare professional, are extremely important.

Menicon Z™(tisilfocon A) contact lenses are indicated for **daily wear or extended wear**. The **maximum** suggested wearing time for these lenses is:

Daily Wear (During Waking Hours)*

Day	Hours
1	4-8
2	6-10
3	8-14
4	10-15
5	12-all waking hours
6 and after -	all waking hours

* If the lenses continue to be well tolerated.

PREPARING AN RGP LENS FOR FITTING

Menicon Z™ (tisilfocon A) Contact Lenses should be thoroughly cleaned with the recommended cleaning solution and hydrated in the desired soaking/conditioning solution for at least 4 hours prior to placement on the eye to insure maximum surface wettability.

CLINICAL STUDY RESULTS:

Study Description:

Six hundred sixty-one (661) subjects were enrolled into a pre-market clinical trial at 24 investigational sites throughout the United States of America. Of those, 630 subjects were determined to be evaluable.

This trial was a multi-center, prospective, open-label, concurrent cohort controlled clinical trial with subjects followed for up to one year. Subjects were assigned either the Menicon Z™ RGP contact lenses or the control soft (hydrophilic) contact lenses based upon their previous lens experience. A total of 317 evaluable Test subjects (Menicon Z) and 313 evaluable Control subjects were recruited. Subjects wore their assigned lenses bilaterally for the duration of the trial.

The Test and the Control lenses were worn on a daily wear schedule for at least 2 weeks prior to advancing to the extended (continuous wear) schedule. The extended wearing schedule for the Test lenses was up to 30 days/29 nights of continuous wear. The Control lenses were worn on an extended wear schedule of up to 7 days/6 nights of continuous wear. The Test subjects replaced their lenses only when needed for cause. The Control subjects replaced their lenses on a weekly basis.

A total of 258 Test subjects (516 eyes) and 210 Control subjects (420 eyes) completed the study. Fifty-nine (59) of the Test subjects (118 eyes) and 103 of the Control subjects (205 eyes) discontinued from the study.

Subject Assessments

Subjects were evaluated upon enrollment to determine eligibility, then scheduled for a dispensing visit. Once dispensed the lenses, subjects were instructed to wear their lenses on a daily wear basis until the 2 week visit, at which time they were evaluated to determine if they could begin extended wear. Once extended wear was initiated, the subjects were evaluated at an optional 24-72 hour visit, and then at the 1 week, 1 month, 3 month, 6 month, 9 month and 12 month visits.

Demographic Data

The Test and the Control groups were similar in regard to gender, medication use, proportion of smokers and average daily wearing time. Differences between the groups are related to the differences in the overall population of rigid gas permeable (RGP) and soft contact lens (SCL) wearers. The Test (RGP) lens subjects were significantly older (an average of 6 years) with a longer history of contact lens wear as compared to the Control (SCL) lens subjects. All subjects recruited were adapted full-time daily wearers of the appropriate lens modality who had no previous extended wear experience.

Gender distribution was similar between the Test and the Control cohorts with a female to male ratio of 2.7 to 1 for the Test cohort and 2.8 to 1 for the Control cohort.

DATA ANALYSIS AND RESULTS

The study was designed to evaluate the equivalence of the Test lens when worn on an extended wear basis for up to 30 days/29 nights to the Control lens when worn on an extended wear basis for up to 7 days/6 nights.

Primary Safety Endpoints

The primary safety endpoint analysis was based upon a comparison between the Test and the Control cohorts of the proportion of visual acuity changes and slit lamp findings.

Visual acuity change criteria included:

- Reductions of best corrected visual acuity (BCVA) by 2 or more Snellen lines from the dispensing BCVA; or
- a decrease in BCVA to worse than 20/40.

The analysis of slit lamp findings as safety criteria is based on the following 5 signs:

- infiltrates of grade 3 or 4;
- corneal staining of grade 3 or 4;
- corneal edema of grade 3 or 4
- giant papillary conjunctivitis (GPC) of grade 3 or 4;
- neovascularization of more than 1.5 mm in a single quadrant or more than 1.0 mm in multiple quadrants

The analysis of the study results indicated no significant difference between the Test lenses and the Control lenses in respect to the safety endpoints. One (1) completed Test subject had one incidence of a decrease in BCVA in the right eye that subsequently returned to the baseline BCVA. Twenty (20) subjects in the Test cohort (6.3%) and 16 subjects in the Control cohort (5.1%) met the slit lamp criteria in either eye at any of their study visits. These percentages were not statistically significantly different ($p=0.50$). The event rate (event in either eye) for the Test cohort was 11.8 per 1000 patient visits and for the Control cohort was 10.8 per 1000 patient visits. This event rate is not statistically different ($p=0.70$).

The Test lens was found to be statistically equivalent to the Control lens in terms of the safety endpoints.

Secondary Safety Endpoints

For all grades of slit lamp findings, extended wear was associated with higher rates of positive findings than daily wear in several categories. The percentages of positive findings for these categories throughout the extended wear phase of the study are as follows: epithelial microcysts (1.6% in Test, 7.0% in Control), epithelial edema (1.1% Test, 3.6% Control), stromal edema (0.3% Test, 1.1% Control), corneal staining (12.4% Test, 17.4% Control), and 3 & 9 o'clock staining (22.2% Test, 0.4% Control).

In both daily and extended wear, neovascularization and palpebral conjunctival abnormalities were noted more often in soft lens wearers, with 3 & 9 o'clock staining noted more often in RGP lens wearers.

Primary Efficacy Endpoints

Efficacy endpoints were set as the percentage of subjects achieving and maintaining the targeted extended wearing time schedule of 30 days/29 nights for the Test cohort and 7 days/6 nights for the Control cohort. Completion of the study was defined as completion of the 12 month follow-up period with the appropriate evaluations performed.

Average Wearing Time

Average wearing times of 22 days or more were reported at 66.5% of all visits after 1 month. 15.5% of wearing time reports were for periods of 8-21 days and 18% of wearing time reports were for periods of less than 8 days.

Adverse Effects

Sixty-three adverse events were reported during the clinical study. Of these, 27 were reported for the Test cohort and 36 were reported for the

Contact Lenses.

Lens Wearing Precautions:

- Never wear lenses beyond the period recommended by the eyecare professional.
- If the lens sticks (stops moving) on the eye, follow the recommended directions on Care for a Sticking (Non-Moving) Lens. The lens should move freely on the eye for the continued health of the eye. If nonmovement of the lens continues, the patient should be instructed to immediately consult his or her eyecare professional.
- Avoid all harmful or irritating vapors and fumes while wearing lenses.
- If aerosol products such as hair spray 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. 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 lens manufacturer or your eyecare professional.

Topics to Discuss with the Patient:

- As with any contact lens, follow-up visits are necessary to assure the continuing health of the patient's eyes. The patient should be instructed as to a recommended follow-up schedule.
- Patients should be advised about wearing lenses during water activities and other sports. Exposing contact lenses to water during swimming or while in a hot tub may increase the risk of eye infection from microorganisms.
- Always contact the eyecare professional before using any medicine in the eyes.
- Certain medications may cause dryness of the eye, increased lens awareness, lens intolerance, blurred vision or visual changes. These include, but are not limited to, antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, oral contraceptives and motion sickness medications. Caution patients using such medications accordingly and prescribe proper remedial measures.

Who Should Know That the Patient is Wearing Contact Lenses:

- Patients should inform the doctor (health care professional) about being a contact lens wearer.
- Patients should always inform the employer of being a contact lens wearer. Some jobs may require use of eye protection equipment or may require that the patient not wear contact lenses.

ADVERSE REACTIONS:

The patient 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
- Abnormal feeling that something is 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 the above, he or she should be instructed to:

- **Immediately remove lenses.**
- 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 eyecare professional. If the lens has dirt, an eyelash, or other foreign body on it, or the problem stops and the lens appears undamaged, the patient should thoroughly clean, rinse, and disinfect the lenses; then reinsert them. After reinsertion, if the problem continues, the patient should **immediately remove the lenses and consult the eyecare professional.**

If the above symptoms continue after removal of the lens, or upon reinsertion of a lens, or upon insertion of a new lens, the patient **should immediately remove the lenses and contact his or her eyecare professional** or physician, who must determine the need for examination, treatment or referral without delay (See Important Treatment Information for Adverse Reactions). A serious condition such as infection, corneal ulcer, corneal vascularization, or iritis may be present and may progress rapidly. Less serious reactions such as abrasions, epithelial stinging or bacterial conjunctivitis must be managed and treated carefully to avoid more serious complications.

Important Treatment Information for Adverse Reactions

Sight-threatening ocular complications associated with contact lens wear can develop rapidly, and therefore early recognition and treatment of problems are critical. Infectious corneal ulceration is one of the most serious potential complications, and may be ambiguous in its early stage. Signs and symptoms of infectious corneal ulceration include discomfort, pain, inflammation, purulent discharge, sensitivity to light, cells and flare, and corneal infiltrates.

Initial symptoms of a minor abrasion and an early infected ulcer are sometimes similar. Accordingly, such epithelial defect, if not treated properly, may develop into an infected ulcer. In order to prevent serious progression of these conditions, a patient presenting symptoms of abrasions or early ulcers should be evaluated as a potential medical emergency, treated accordingly, and be referred to a corneal specialist when appropriate. Standard therapy for corneal abrasions such as eye patching or the use of steroids or steroid/antibiotic combinations may exacerbate the condition. If the patient is wearing a contact lens on the affected eye when examined, the lens should be removed immediately and the lens and lens care products retained for analysis and culturing.

designs should always be considered when fitting patients for extended wear. Deswelling rates with RGP lenses have been shown to be rapid and nearly complete within the first three hours of awakening. The prescribing eye care professional should carefully assess the potential impact of these factors and carefully monitor the continuing ocular health of the patient and lens performance on the eye.

- The potential impact of these factors on the patient's ocular health should be carefully weighed against the patient's need for refractive correction; therefore, the continuing ocular health of the patient and lens performance on the eye should be carefully monitored by the prescribing eyecare professional.
- The following patients may not be suitable extended wear contact lens candidates, and/or may experience a higher rate of adverse effects associated with contact lens wear:
 - Patients with a history of acute inflammatory reactions to contact lens wear.
 - Patients with a history of giant papillary conjunctivitis associated with contact lens wear.
 - Patients with a history of ocular allergies may need to temporarily discontinue lens wear during certain times of the year.
 - Patients with a history of non-compliance with contact lens care and disinfection regimen, wearing restrictions, wearing schedule, or follow-up visit schedule.
 - Patients who are unable or unwilling to understand or comply with any directions, warnings, precautions, or restrictions. Contributing factors may include but are not limited to age, infirmity, other mental or physical conditions, and adverse working or living conditions.
 - Patients who are unwilling or unable to adhere to a recommended care regimen, or who are unable to insert and remove lenses, should not be provided with them.
- Eyecare professionals should instruct the patient to remove the lenses immediately if the eye becomes red or irritated.
- The use of fluorescein is contraindicated in those persons who have a known hypersensitivity to any component.
- The presence of the ultraviolet (UV) light absorber in the Menicon Z™ (tisilfocon A) Contact Lens material may require equipment enhancement to visualize fluorescein patterns adequately. (Refer to the Fitting Guide for detailed instructions.)
- Some patients will not be able to tolerate continuous wear even if able to tolerate the same or another lens on a daily wear basis. Some patients who are able to tolerate continuous wear will not be able to wear their lenses continuously for 30 days. Patients should be carefully evaluated for continuous wear prior to prescription and dispensing, and eyecare professionals should conduct early and frequent follow-up examination to determine ocular response to continuous wear.
- As with any contact lens, follow-up visits are necessary to assure the continuing health of the patient's eyes. The patient should be instructed as to a recommended follow-up schedule.
- Aphakic and other post-surgical persons should not be fitted with Menicon Z™ (tisilfocon A) Contact Lenses until the determination is made that the eye has healed completely.
- Lenses are shipped in a plastic container immersed in Alcon® Unique-pH™ Multi-Purpose Solution. If the plastic container has missing solution or is dry, return the product to the Authorized Manufacturing Lab according to their return policies.
- If continual wet storage of wet shipped contact lenses is preferred, the Alcon® Unique-pH™ Multi-Purpose Solution should be changed every 30 days from the hydration date.
- If the patient is sensitive to edetate disodium or polyquaternium-1, the lens should be removed from the vial upon receipt, rinsed with fresh saline solution, cleaned with a cleaner and placed in another prescribed disinfecting solution prior to dispensing. Follow the manufacturer's instructions on the disinfecting solution label.
- Patients who wear aspheric contact lenses to correct presbyopia may not achieve the best-corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.

Eyecare professionals should carefully instruct patients about the following care regimen and safety precautions. It is strongly recommended that patients be provided with a copy of the Patient Instructions for the Menicon Z (tisilfocon A) Rigid Gas Permeable Contact Lens available from Menicon and understand its contents prior to dispensing the lenses.

³Investigative Ophthalmology and Visual Science, October 1984; Vol 25, pp. 1161-1167

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-based cosmetics are less likely to damage lenses than oil-based products.
- Before leaving the eyecare professional's office, the patient should be able to promptly remove lenses or should have someone else available who can remove the lenses for him or her.
- Do not touch contact lenses with the fingers or hands if the hands are not free of foreign materials, as microscopic scratches of the lenses may occur, causing distorted vision and/or injury to the eye.
- Always handle lenses gently and avoid dropping them on hard surfaces.
- Do not touch the lens with fingernails.
- Carefully follow the handling, insertion, removal, cleaning, disinfecting, storing and wearing instructions in the Patient Instructions for the Menicon Z™ (tisilfocon A) Contact Lens and those prescribed by the eyecare professional.
- Never use tweezers or other tools to remove lenses from the lens container unless specifically indicated for that use.

Solution Precautions:

- Always use fresh unexpired lens care solutions.
- Always follow directions in the package inserts for the use of contact lens solutions.
- Sterile unexpired solutions, when used, should be discarded after the time specified in the labeling directions.
- Always keep the lenses completely immersed in the recommended storage solution when the lenses are not being worn (stored). Prolonged periods of drying may reduce the ability of the lens surface to return to a wettable state.
- Do not use saliva or anything other than the recommended solutions for lubricating or wetting lenses.
- Different solutions cannot always be used together, and not all solutions are safe for use with all lenses. Use only recommended solutions.
- Do not heat the cleaning, wetting, and/or soaking solution and lenses. Keep away from extreme heat.
- Use only a chemical (not heat) lens care system. Use of a heat (thermal) care system can damage the Menicon Z™ (tisilfocon A)