

SUMMARY OF SAFETY AND EFFECTIVENESS

I. General Information

- A. Device Generic Name: Tisilfocon A Rigid Gas Permeable Contact Lens
- B. Device Trade Name: Menicon ZTM (tisilfocon A) Rigid Gas Permeable Contact Lenses
- C. Applicant's Name and Address: Menicon U.S.A., Inc.
333 West Pontiac Way
Clovis, CA 936120-5613
- D. Premarket Approval (PMA) Application Number: P990018
- E. Date of Notice of Approval to Applicant: JUL 11 2000

II. Indications for Use

Menicon ZTM (tisilfocon A) spherical, aspheric prism ballast, toric and 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 ZTM (tisilfocon A) spherical or aspheric lenses and non-prism ballast toric lenses are indicated for extended wear (from 1 to 7 days between removals for cleaning and disinfection of the lenses, as recommended by the eyecare practitioner) for the correction of refractive error (myopia, hyperopia, presbyopia and/or astigmatism) in non-aphakic persons with non-diseased eyes.

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

(*The Menicon ZTM (tisilfocon A) lens was cleared for daily wear under K962006 on October 9, 1996.)

III. Device Description

Menicon ZTM rigid gas permeable contact lens is a lathe cut non-polished firm contact lens with spherical or aspherical back surfaces. The posterior curve is selected to fit the individual eye, and the anterior curve is selected to provide the necessary optical power to correct the refractive error. A peripheral curve system on the posterior surface allows tear exchange between the lens and cornea.

The lens material (tisilfocon A) is a thermoset copolymer derived from fluoro-methacrylate and siloxanylstyrene, bound by crosslinking agents. The lens is available in a light blue tint. The lens is tinted with color additive D& C Green No. 6. The UV absorber Benzotriazol is incorporated as an additive during the manufacturing process. The lens may be prescribed for extended wear in powers ranging from -20.00 D to +12.00 D, in 0.25 D steps.

IV. Contraindications and Warnings

Please refer to approved labeling.

V. Alternate Practices and Procedures

The alternate practices and procedures to the Menicon Z™ Rigid Gas Permeable Contact Lens are soft (hydrophilic) daily wear and extended wear contact lenses, daily wear rigid gas permeable lenses, radial keratotomy, photorefractive keratectomy, LASIK, intrastromal corneal rings or spectacles.

VI. Marketing History

Menicon Z (tisilfocon A) RGP lenses have been marketed in the following countries: Japan, France, Germany and the United States. The marketing history of each country is addressed below.

A. Japan

Menicon Co., Ltd. received marketing approval for Menicon Z™ RGP Contact Lenses from the Japanese Ministry of Health and Welfare in August 1995. The approval number was 20700BZZ00739000. The approval included both daily and extended wear (up to 7 days) indications. Commercial marketing of the Menicon Z™ lens began in April 1996. As of January 1999, approximately 700,000 lenses have been sold in Japan. Neither serious adverse reactions nor serious complaints have been filed or reported.

B. France and Germany

Menicon Co., Ltd. began marketing Menicon Z™ lenses in France in July 1997. As of January 1999, Menicon has sold approximately 38,000 lenses in this market for daily wear and extended wear. Neither serious adverse events nor complaints have been filed or reported.

Menicon Co., Ltd. began marketing Menicon Z™ lenses in Germany in October 1997. As of January 1999, Menicon Co., Ltd. has sold approximately 23,500 lenses in this market for daily wear and extended wear. Neither serious adverse events nor complaints have been filed or reported.

C. United States

Menicon Co., Ltd. received 510(k) clearance from FDA in October 1996 for the daily wear of Menicon Z™ lenses. As of January 1999, Menicon Co., Ltd. has sold approximately 76,000 lenses in the United States.

Four MDR reports have been filed for the Menicon Z lens in the US. There were three complaints of lens breakage with no injury. In the first complaint, the lens broke in the person's eye. In two additional complaints, the lens broke upon removal. No lens defects were found on the lens which was evaluated. The other lens could not be evaluated; however, no manufacturing problem was noted. In a fourth MDR, eye irritation was attributed to an unusual manufacturing problem.

VII. Potential Adverse Effects of the Device on Health

Potential adverse effects on health associated with extended wear contact lenses include eye problems such as corneal ulcers, epithelial microcysts, infiltrates and endothelial polymegathism. The risk of corneal ulcer has been shown to be greater among users of extended wear contact lenses than among users of daily wear contact lenses. The risk among extended wear lens users increases with the number of consecutive days that the lenses are worn between removals, beginning with the first overnight use. Strict compliance with the proper lens care regimen and wearing schedule is essential in minimizing risk.

VIII. Summary of Preclinical Studies

The objective of the preclinical studies was to provide reasonable assurance of the safety of the Menicon Z lens prior to clinical testing.

A. Biocompatibility Testing

The following toxicology tests were performed: Systemic Injection Toxicity Test, Ocular Irritation Test, Cytotoxicity Test and Three Week Ocular Safety Test. The test results raise no acute toxicological concerns and support the safety of the study lens for its intended use.

B. Compatibility Testing

A study was conducted to evaluate the compatibility of Menicon Z™ (tisilfocon A) RGP contact lens with the following care systems: Advance System, OPTI-SOAK™ System, ComfortCare System, SIMPLICITY and CLARIS Cleaning and Soaking Solution. This testing was conducted in accordance with the FDA recommended method in the Guidance Document for Class III Contact Lenses, April 1989. All care systems tested were compatible with the Menicon Z™ RGP contact lens.

C. Physical and Optical Parameters

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:	1) Claris Cleaning and Soaking Solution below 20 degree (Dry state after plasma treatment) 19 ± 1.5 degree (after soaking period of 7 days) 2) Comfort Care GP Wetting & Soaking Solution below 15 degree (Dry state after plasma treatment) 25 ± 1.4 degree (after soaking period of 7 days)
Light Transmittance:	Visible region: $>95\%$ (380-780 nm) sample thickness (0.8 mm) Ultraviolet region: $<6\%$ (210 nm – 380 nm)
Water Absorption:	Less than 0.5% by weight
Oxygen Permeability:	$163 \pm 4.1 \times 10^{-11}$ (cm ² /sec)(mL O ₂ /(mL x mmHg) Dk

D. Lens Stability

One month stability studies have been conducted on the non-sterile Menicon Z™ RGP lens packaged in Barnes-Hinds Comfort-Care Wetting and Soaking Solution. The data supports a storage time of up to 30 days. Lenses are cleaned and disinfected prior to dispensing.

E. Evaluation of Menicon Z Packaging Materials

Toxicology testing of the cap and holder as well as the bottle was performed. This testing included the following tests: Acute Systemic Toxicity Test, Ocular Irritation Test, Cytotoxicity Test and MEM Elution Test. Each component of the shipping case showed non-significant toxic reaction in comparison to the negative control.

F. Bioburden Evaluation

Bioburden evaluations were conducted on lenses packaged in the dry state and lenses packaged in the wet state. Bioburden levels of dry lenses were evaluated following packaging and each time point evaluated in the stability study. Bioburden levels of wet lenses were evaluated following initial packaging and after 30 days. In all instances, bioburden levels were found to be below 100 CFU/lens.

G. Conclusion of Preclinical Studies:

The results of the preclinical studies provided reasonable assurance that the Menicon Z™ RGP Contact Lens was safe for use for its intended use.

IX. Summary of Clinical Studies

The clinical study was designed according to the FDA Guidance Document for Class III Contact Lenses, April 1989.

A. Study Objective

The objective of this clinical study was to demonstrate in a comparative trial the safety and efficacy of Menicon Z™ RGP Contact Lens for extended wear for up to 7 days in the correction of visual acuity of nondiseased eyes that are myopic with an astigmatism of up to 3.00 D. The primary objective is to determine equivalence to the control lens.

B. Study Design:

This was a prospective, multicenter comparative trial, using as a historical control the Menicon SF-P™ for up to 7 days extended wear. The control lens was approved in P880098/S1 on February 8, 1990. A total of 520 eyes were dispensed trial lenses by 8 investigators (enrollment ranged from 159 eyes to 1 eye).

C. Study Population

A total of 520 eyes (261 subjects) were dispensed trial lenses by eight (8) investigators in this clinical study. Of the 520 eyes fitted and dispensed lenses, 77.7% completed the study and 22.3% discontinued from the study prematurely.

The exclusion criteria were: lid or conjunctival abnormality or infection, history of iritis, astigmatism >3D, ocular or systemic disease or medications that contraindicate CL wear, sensitivity to CL care products, pregnancy, enrollment in another clinical trial. The inclusion criteria were: need optical correction, no significant residual astigmatism, correctable to 20/40, healthy eyes, no ocular medications, clear cornea without clinically significant slit lamp findings, willingness to follow-up and adhere to the protocol, and informed consent.

The mean age of study eyes was 40.4 years. The mean age among completed eyes was 41.0 years while the mean age among discontinued eyes was 38.2 years. Most eyes (69.8%) were female (69.3% completed eyes and 71.6% discontinued eyes). In addition, most eyes (92.3%) were Caucasian. Of the remainder, 3.8% were Asian, 2.3% were Hispanic, and 1.5% were Black. Of the completed eyes, 95.5% had previous lens wearing experience and 87.9% of the discontinued eyes had previous contact lens wearing experience.

The comparison group of 286 historic controls from the Menicon SF-P™ RGP contact lens had a mean age of 35.2 years. Approximately 70% of the patients were female.

D. Study Period

The Menicon Z study was initiated in August 1995. The reporting period was twelve (12) months. The last observation made in February 1997.

E. Findings

1. Safety

The safety of the lens was evaluated primarily in terms of the incidence and severity of unanticipated adverse reactions; slit lamp findings; and symptoms, problems and complaints. Further assessment of safety was based on the incidence of significant keratometry changes and decreases in visual acuity of 2 or more Snellen lines. Reasons for discontinuation from the study and frequency of lens replacement were also evaluated.

a. Unanticipated Adverse Reactions

There were no unanticipated adverse device effects during the study.

b. Slit Lamp Findings

The results of slit lamp examinations performed at each follow-up visit were graded according to the FDA recommended classification scheme. Grade 4 classification (severe) was not reported at any time during the study by either of the study completed groups or the discontinued group. Overall, 4 eyes (0.8%) had grade 3 or worse findings at any time during the study, compared with 12 eyes (4.3%) of the historical control group. Based on statistical testing, the Menicon Z™ CL is equivalent to the control CL in the proportion of grade 3 or worse slit lamp findings.

- corneal edema – Among completed eyes, 0.2% had grade 3 (control 0.7%).
- staining – Among completed eyes, 0.2% had grade 3 (control 3.5%).
- neovascularization – Among completed eyes, 3 cases reported: two grade 1, and one grade 2. None were grade 3 (control 0.4%).
- bulbar and limbal injection – Among completed eyes, 2 (0.5%) transient cases reported: one SCH/episcleritis and one allergic reaction to wool (control 0%).
- iritis – none reported (control 0%).
- tarsal abnormalities – none reported (control 0%).
- “other” – Among completed eyes, most prevalent findings were faint compression ring, epithelial basement membrane dystrophy, and conjunctival staining. None were grade 3.

A total of 27 subjects reported wearing their lenses OU >7 days between removal (range 8 to 30 days). Positive slit lamp findings in these eyes included: none

(majority), corneal staining and edema (only 1 event was grade 3), and limbal injection.

c. Subjective Symptoms, Problems and Complaints (SPC)

None of the reported SPC's required treatment. Among completed eyes, only 4 categories occurred with an incidence of >10%. Overall, comparison to discontinued eyes by visit revealed no notable increase for any SPC. At 12 months, 33.4% of completed eyes had 1 or more SPC (36.5% of total visits).

- lens awareness – 20.1% completed eyes at 1 year reported some level of lens awareness, 0.5% severe. At any scheduled visit, no more than 0.6% reported severe. No trends over time were noticed. Discontinued eyes ranged from 56.8% (2 hours) to 16.7% (9 months).
- discomfort – 15.1% of completed eyes at 1 year reported some level of discomfort, 0.7% severe. No trends over time were noticed. At any scheduled visit, no more than 0.7% reported severe. Discontinued eyes ranged from 58.3% (1 month) to none (9 months).
- burning/itching – 12.9% of completed eyes at 1 year reported some level of burning/itching, 0.2% reported as severe. At any scheduled visit, no more than 1.3% reported severe. Discontinued eyes ranged from 0% (9 months) to 33% (1 month).
- “other” – most prevalent were dryness, “filmy,” and CL prescription-related problems. 7.1% of completed eyes at 1 year reported some level of “other” symptoms. Discontinued eyes ranged from 0% (9 months) to 40% (5 months).

Reports for all categories were fewer or comparable to the historical control. Of all SPC's, spectacle blur showed the greatest disparity between groups for all cases (18% trial lens, 31.9% control), and for severe cases (0.4% trial, 3.7% control). “Flare” (13.6% trial, 22% control), variable vision (29.8% trial, 38.8% control), and distance blur (29.3% trial, 37.7% control) were the 3 next most discrepant SPC's.

d. Keratometry Results

The keratometry results of the Menicon Z™ lens were not worse than the results for the Menicon SF-P™ contact lens historical control group.

e. Refractive Changes

Of the 520 eyes, 2.1% had a refractive change (cylinder diopter) > 1.00 D. The maximum cylinder change was 2.5 D. Refractive change measured by sphere diopter was more than one diopter for 3.1% eyes. The maximum sphere change was 2.0 D.

f. Decrease of 2 or More Snellen Lines in Visual Acuity

Among eyes bcorrected for far visual acuity in the Menicon ZTM contact lens group, 5 completed and 3 discontinued eyes experienced a decrease of 2 or more Snellen lines throughout the study. A comparable proportion of eyes in both the Menicon ZTM contact lens group and the Menicon SF-PTM contact lens historical control group experienced a decrease of 2 or more Snellen lines.

g. Study Discontinuation

During the Menicon ZTM contact lens study 116 (22.3%) of the eyes discontinued. Of the 22.3% discontinued, most were for unacceptable comfort (9.6%) or lost to follow-up (6.9%). There were no statistically significant differences between the Menicon ZTM contact lens group and the Menicon SF-PTM contact lens historical control group in the proportions of discontinued patients.

h. Lens Replacements

There were more lens replacements in the Menicon SF-PTM contact lens historical control group (56.3% of eyes with at least one replacement) than in the Menicon ZTM contact lens group (35.8% of eyes). The most common reasons for lens replacement were lost/misplaced lens and incorrect power/base curve.

2. Efficacy

The effectiveness of the lens was evaluated primarily in terms of visual acuity results at the 12 month follow-up visit and lens wearing time.

a. Visual Acuity

After 12 months of contact lens wear, 99.7% of eyes corrected for far acuity had a lens visual acuity of 20/40 or better. These results are comparable to the proportion of eyes in the Menicon SF-PTM contact lens historical control group with final lens visual acuity results of 20/40 or better after 12 months of lens wear (99.5%). Based upon these results and statistical testing, the Menicon ZTM lens is equivalent to the Menicon SF-PTM in the correction of visual acuity.

b. Lens Wearing Time

After 12 months of contact lens wear, the mean number of days between removals for the Menicon ZTM contact lens group was 6.4 days with approximately 80% achieving 7 days between removals. The mean number of days between removals was 6.5 days for the historical control with approximately 63% achieving 7 days between removals.

F. Conclusion of Clinical Study:

The experience of eyes wearing the Menicon Z™ Contact Lens was comparable to or better than the experience of the eyes in the historical control group with respect to most clinically significant safety data evaluated (e.g., unanticipated adverse events and slit lamp findings Grade 3 or higher).

Efficacy results based on 12 months of lens wear demonstrate that the efficacy and safety of the Menicon Z™ Contact Lens is comparable to that of the Menicon SF-P™ historical control group.

X. Conclusion Drawn from the Studies:

The results of the preclinical and clinical studies provide reasonable assurance of the safety and effectiveness of Menicon Z™ (tisilfocon A) Rigid Gas Permeable Contact Lens for the patient population, refractive conditions, and specified duration of wear. Although the potential exists for minor differences in physiological response by gender for the target population, the minimal number of clinically significant findings does not indicate that gender differences are of clinical importance for this device.

XI. Panel Recommendation

This PMA was not referred to the Ophthalmic Devices Panel for review and recommendation because the Panel has previously reviewed similar information.

XII. FDA Decision

FDA issued an approval order on **JUL 3 2000**

The manufacturing facility was found to be in compliance with device Good Manufacturing Practices (GMP). Final GMP approval was dated