

# A two-week clinical evaluation of the safety of Systane<sup>®</sup> Ultra in contact lens-wearing patients

David Kading

Specialty Eyecare Group,  
Kirkland, WA, USA

**Objective:** To evaluate the safety of Systane<sup>®</sup> Ultra Lubricant Eye Drops (test solution) in contact lens wearers. A currently marketed contact lens rewetting drop was the control solution.

**Participants:** This investigator- and patient-masked, single-site, randomized, and prospective study involved 45 successful contact lens wearers.

**Methods:** Eligible subjects' baseline biomicroscopy findings, visual acuity, and corneal staining score were recorded. Subjects received either the test or control solution with masked labeling. Subjects were instructed to instill their assigned solution in both eyes: 15 minutes prior to lens insertion, at least one drop during lens wear and another drop immediately following lens removal. After 14 days, biomicroscopy results, visual acuity, and corneal staining score were recorded.

**Results:** No adverse events were documented for either the test or the control solution. For subjects using Systane<sup>®</sup> Ultra, no statistically significant change was detected in visual acuity ( $= 0.7667$ ) or corneal staining score ( $P = 1.000$ ). For subjects using the control solution, the change in visual acuity ( $P = 0.0011$ , mean difference  $= 1.70 \pm 3.22$  standard deviation) was not clinically relevant and there was no significant change in corneal staining score ( $P = 0.5413$ ).

**Conclusions:** This clinical study provided evidence of safety and compatibility of Systane<sup>®</sup> Ultra Lubricant Eye Drops in contact lens wearers.

**Keywords:** lubricant eye drop, contact lens, safety, dry eye

Contact lens wear continues to be a popular method of vision correction, with an estimated 35 million contact lens wearers in North America.<sup>1</sup> New lens polymers that promote ocular health, longer-lasting comfort, and flexible wearing modalities attract new wearers and contribute to the success of this form of vision correction.

Despite the fact that the contact lens market is growing, a concerning number of contact lens wearers drop out of contact lens wear every year. While inconvenience, ocular hyperemia, blurry or inconsistent vision as well as cost are all factors in an individual's decision to discontinue lens wear, contact-lens induced dryness and discomfort are consistently reported as the most common reasons for lens abandonment.<sup>2,3</sup> Pritchard and colleagues found 12% of contact lens patients discontinued lens wear within five years of the initial fitting due to dryness and discomfort symptoms.<sup>4</sup>

For patients, 'discomfort' and 'dryness' are often synonymous, with a high correlation between comfort and dryness ratings for both symptomatic and asymptomatic patients.<sup>1</sup> Among current contact lens wearers, approximately 50% experience dry eye symptoms to varying degrees. And while, in most cases, the dryness is not frequent

Correspondence: Dave Kading  
11830 NE 128th St, Suite 1,  
Kirkland, WA 98034, USA  
Tel +1 425 821 8900  
Fax +1 425 814 9782  
Email doctorkading@gmail.com.

or noticeable enough for wearers to remove their lenses, as many as 20% have symptoms severe enough for them to reduce their wearing time.<sup>5,6</sup> In a study of 1,054 patients surveyed on dry eye symptoms (including 367 contact lens wearers), the authors report an even higher incidence of ocular dryness. Of the contact lens wearers surveyed, 77% reported some degree of dryness symptoms (compared to nearly 44% of nonlens wearers). In addition, 70% to 80% of the contact lens wearers reported frequent eye discomfort and visual changes.<sup>7,8</sup>

The reported effects of contact lenses on the tear film may precipitate dry eye symptoms. A reduction in the pre-lens tear film lipid layer and an increase in tear film evaporation are associated with contact lens wear.<sup>9–13</sup> These changes result in increased tear film osmolality<sup>14,15</sup> affecting tear film stability and tear break up time. This disruption of the tear film in contact lens wearers is associated with reduced functional visual acuity,<sup>16,17</sup> decreased wear time<sup>4</sup> and an increased risk of ocular surface desiccation.<sup>18,19</sup>

Artificial tear supplements are widely used to relieve dry eye symptoms and sustain ocular comfort during lens wear.<sup>20</sup> Begley and colleagues report that 47% of contact lens wearers reported the use of rewetting drops but indicated that these provided only moderate relief.<sup>7</sup> Despite their viscosity-enhancing ingredients, instilled drops tend to have a short residency time and require frequent re-instillation throughout the day.

Systane<sup>®</sup> Ultra Lubricant Eye Drops (Alcon Laboratories, Inc., Fort Worth, TX, USA) is a new-generation ocular lubricant for the treatment of dry eye. Clinical results show that Systane<sup>®</sup> Ultra provides long lasting relief from dry eye.<sup>21,22</sup>

The loosely cross-linked, droppable gel, after instillation in the eye, reduces in viscosity with the first blink allowing even distribution over the ocular surface. Subsequent interaction with the divalent ions and mucin in the tear film facilitates the development of a viscoelastic, gel-matrix with shear thinning and bioadhesive properties. The gel-matrix promotes retention of the active demulcents for tear film stability, lubrication, and protection of the ocular surface.<sup>23,24</sup>

The clinical benefits of Systane<sup>®</sup> Ultra in treating dry eye together with its viscoelastic properties may offer advantages for contact lens wearers in the prevention of contact lens-related dry eye.

The purpose of this clinical study is to evaluate the safety of Systane<sup>®</sup> Ultra in a group of successful contact lens wearers compared with that of a currently available contact lens rewetting drop: Sensitive Eyes<sup>®</sup> Rewetting Drops (Bausch and Lomb, Rochester, NY, USA).

## Methods

### Materials

The test solution was Systane<sup>®</sup> Ultra Lubricant Eye Drops containing polyethylene glycol 400 (PEG) and propylene glycol (PPG) as demulcents. Bausch and Lomb Sensitive Eyes<sup>®</sup> Rewetting Drops, an isotonic aqueous solution with low viscosity, currently marketed as a drop to reduce contact lens-related dryness symptoms, was used as the control solution.

### Study population

This prospective, randomized, double-masked, single site clinical study of two weeks duration enrolled 45 successful contact lens wearers aged between 18 and 65 years wearing either once or twice per month planned-replacement soft contact lenses (SCL) or gas permeable (GP) lenses. As a prerequisite for enrollment, subjects were required to have contact lens acuity of 20/30 or better in each eye, be in good health and to continue any pre-enrollment systemic medication regimens during the study. Attendance at all clinical study visits and completion of study questionnaires was also required. There were no restrictions to the currently employed contact lens care regimen, rewetting drop usage or lens type (planned replacement soft or GP).

Exclusion criteria included a history of allergy to any study product ingredient and current use of any topical eye medications (with the exception of rewetting drops or artificial tear products). Subjects who had modified their systemic medications within 30 days prior to enrollment were excluded as were subjects with significant active corneal, eyelid or anterior segment infection or inflammation.

The primary objective was to evaluate safety with the use of Systane<sup>®</sup> Ultra in contact lens wearers. A comparison to a currently available contact lens rewetting drop was included as a control. Safety was established by assessment of visual acuity, corneal staining, biomicroscopy examination and adverse events. The clinical study was performed in compliance with the ethical principles of the Declaration of Helsinki and written informed consent was obtained from all patients enrolled.

### Procedures

At the first screening visit (Visit 1 – screening), after a subject's preliminary eligibility was established, demographic information, medical history and current usage of systemic medication and any topical ocular drops (including rewetting drops, artificial tears and Restasis<sup>®</sup> [Allergan, Inc., Irvine

CA, USA]) was recorded. Baseline measurements of safety parameters, including distance visual acuity with contact lenses and corneal staining score were recorded. Biomicroscopy findings (lids/eyelashes, cornea, and conjunctiva) were recorded as either normal or abnormal.

Subsequently, patients were randomly dispensed either Systane® Ultra or Sensitive Eyes. Both the test and the control solutions were dispensed in 10 and 15 mL bottles with sterile closures and masked labeling supplied in pre-numbered kits. Patients were educated in the correct administration of the drops and instructed to instill 1–2 drops of the assigned lubricating eye drop in both eyes on a daily basis, approximately 15 minutes prior to contact lens insertion, at least one drop during the lens wear period and immediately following lens removal. Written instructions were provided.

Follow up visits (Visit 2 – follow up) were conducted two weeks after the first screening visit. Results for distance visual acuity with contact lenses and corneal staining score were recorded. Any changes in biomicroscopy assessment of the lids, cornea, and conjunctiva were recorded. Biomicroscopy findings (lids/eyelashes, cornea, and conjunctiva) were also recorded.

## Distance visual acuity

Contact lens visual acuity was measured for distance. Acuties were measured using a Snellen letter chart. Testing was conducted monocularly under photopic lighting conditions (85 cd/m<sup>2</sup>).

## Biomicroscopy

Subjects were assessed for corneal staining and any abnormal findings associated with the lids, cornea, and conjunctiva. Corneal staining was graded using the NEI staining grid in which a score of 0–3 (0 = normal and 3 = severe) was assigned to each of five corneal regions (nasal, central, temporal, inferior, and superior) with a maximum total score of 15 (Figure 1).<sup>10</sup>

## Adverse events

Adverse events were considered to be any unfavorable or unexpected medical occurrence in a subject using the test or control solutions. For enrolled subjects, any change from baseline in the clinical findings deemed unfavorable, was considered an adverse event and recorded. Serious adverse events, whether related to use of the respective solution or not, required discontinuation of that solution and appropriate medical treatment.

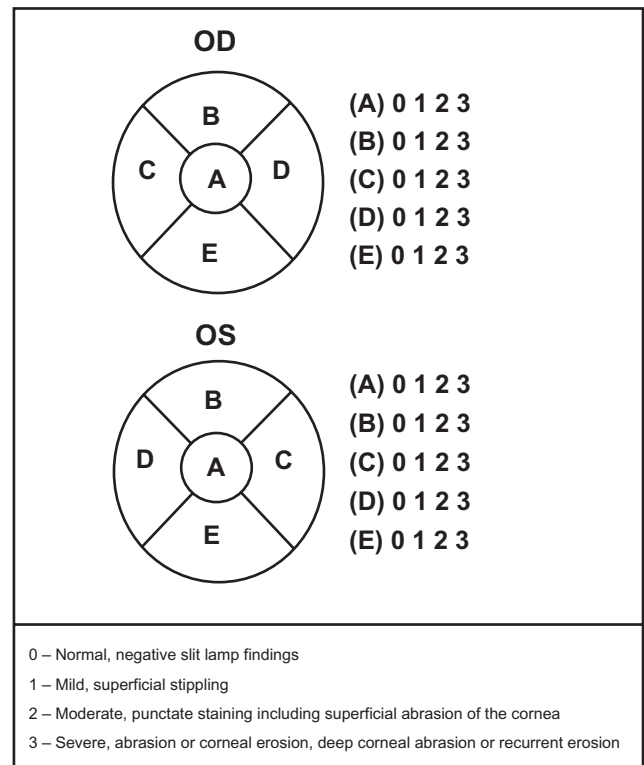
## Statistical methods

Within-subject before and after treatment comparison was conducted using paired *t*-test. Student's *t*-test was used for between-group comparisons in numeric. All tests were two-sided with the confidence level set to 95%.

## Results

Forty-five subjects were enrolled and successfully completed the study. There were 14 (31%) males and 31 (69%) females ranging in age from 21 to 53 years (mean, 31.2 years; standard deviation [SD], 8.1). Subject ethnicity was White (n = 40, 89%), Asian (n = 2), Hispanic (n = 1), and two were unspecified. Twenty-three subjects were randomized into the Systane® Ultra group, and 22 into the Sensitive Eyes® group. The two treatment groups were comparable in demographic background.

Within-subject changes in visual acuity and the corneal staining score are presented in Table 1. No significant changes in visual acuity were observed in the Systane® Ultra group ( $P = 0.7667$ ). In the Sensitive Eyes® group ( $P = 0.0011$ ), an improvement in visual acuity from 22.27 (SD, 3.32) to 20.57 (SD, 1.61) ( $P = 0.0011$ ) was observed, although this is not considered clinically relevant.



**Figure 1** Corneal staining was graded in each of five corneal zones using the NEI grid (superior, nasal, central, inferior, temporal).

## Adverse events

There were no adverse events reported from this clinical study. No clinically significant abnormal biomicroscopy findings were reported during follow-up in either group.

## Discussion

The safety of Systane® Ultra Lubricant Eye Drops in contact lens wearers was evaluated in this clinical study involving 45 successful lens wearers. Systane® Ultra was well tolerated and demonstrated a favorable safety profile when administered topically at least three times a day in conjunction with contact lens wear. Ocular assessments including visual acuity and corneal staining score showed no significant treatment-related changes and there were no serious ocular or systemic adverse events reported. The safety profile of Systane® Ultra was comparable to that of a currently marketed contact lens rewetting drop. These clinical findings add support for the use of Systane® Ultra by contact lens wearers.

These results provide contact lens wearers with increased confidence in the use of Systane® Ultra during lens wear for the treatment of contact lens-related dry eye. Given that dryness is the most frequent symptom in approximately 75% of contact lens wearers<sup>25,26</sup> and contact lens wear can increase the frequency and severity of pre-existing dry eye,<sup>25</sup> there is considerable opportunity for contact lens wearers to experience the relief of an effective dry eye therapy. Additional clinical benefits of Systane® Ultra in dry eye patients, namely, immediate patient comfort, enhanced lubrication and minimal blur on instillation,<sup>27</sup> are likely to also apply to contact lens wearers. Conclusions drawn by Christensen and colleagues regarding the overall safety profile of an hydroxypropyl guar (HP-Guar)-containing lubricant eye drop in prior research<sup>28</sup> add support to the findings of the current study.

Systane® Ultra Lubricant Eye Drops is a new product in the Systane® family of dry eye therapies. It is an aqueous solution comprising PEG (0.4%) and PPG (0.3%) as demulcents and incorporating the benefits of HP-Guar as a gelling agent. The above-mentioned ingredients have a history of use in ophthalmic preparations as well as contact lens care products and have demonstrated compatibility with the ocular surface.<sup>28</sup> In addition, Systane® Ultra includes borate and sorbitol as key ingredients. Sorbitol, a water soluble, nonionic compound, interacts with borate<sup>29</sup> to control viscosity in the bottle for optimal delivery in the eye. The presence of sorbitol facilitates the even distribution of the eye drop over the ocular surface upon instillation.

Ketelson and colleagues<sup>27</sup> demonstrated that this increase in viscoelasticity on-eye and between blinks correlates with a significant reduction in friction. This finding has implications for contact lens wear whereby the reduction in friction between the lens and the lids has the potential to improve lens-wearing comfort. Similar reductions in friction have been reported by Meyer and colleagues in connection with a similar HP-Guar containing ocular lubricant from within the Systane® family.<sup>30</sup> In addition, a study involving contact lens wearers showed that the use of an HP-Guar-containing ocular lubricant was associated with improved comfortable lens-wearing times and an improved overall lens-wearing experience.<sup>31</sup>

The success of contact lens wear depends on the integrity and stability of the tear film. While Systane® Ultra is not considered to be used a re-wetting solution for contact lens wearers, Systane® Ultra is designed to rebuild the tear film for long-term lubrication and extended protection of the ocular surface.<sup>22</sup> A good tear film covering a contact lens is thought to provide comfort, vision, lubrication, prevent surface drying, remove debris, and counter infection.<sup>6</sup> Chalmers and Begley<sup>8</sup>

**Table I** Within-subject changes in visual acuity (Snellen best-corrected visual acuity) and the sum staining score

Time	Systane® Ultra (n = 46 eyes)		Sensitive Eyes® (n = 44 eyes)		P-value <sup>1</sup>
	Mean (SD)	Range	Mean (SD)	Range	
<b>Baseline</b>					
Visual acuity	21.20 (2.40)	20–30	22.27 (3.32)	20–30	0.0826
Sum staining score	0.33 (0.63)	0–2	0.43 (0.76)	0–2	0.4746
<b>Follow-up</b>					
Visual acuity	21.30 (2.46)	20–30	20.57 (1.61)	20–25	0.0951
Sum staining score	0.33 (0.67)	0–3	0.55 (1.02)	0–5	0.2342

**Notes:** P-values of Student's *t*-test for between-group comparison. Per paired *t*-test, no statistically significant within-subject changes were detected for the Systane® Ultra group for visual acuity ( $P = 0.7667$ ) or sum staining scores ( $P = 1.0000$ ). For the Sensitive Eyes group, the changes in visual acuity were statistically significant ( $P = 0.0011$ , mean difference =  $1.70 \pm 3.22$  SD), but not the sum staining score ( $P = 0.5413$ ). Clinically, a change of 1.70 in visual acuity is not considered clinically relevant.



claim that tear film instability is present in almost all contact lens wearers with or without symptoms indicating that the benefits of Systane® Ultra can apply to asymptomatic as well as symptomatic lens wearers.

Moreover, an HP-Guar-containing solution reduced aqueous tear evaporation 30 and 60 minutes after application in dry eye patients. This antievaporative effect may also be achieved in normal eyes when in low relative humidity environments<sup>32</sup> and may therefore offer further advantages to contact lens wearers.

## Conclusion

Systane® Ultra is recommended for the temporary relief of burning and irritation due to dryness of the eye. Use of Systane® Ultra Lubricating Eye Drops in successful contact lens wearers was not associated with any significant change in corneal staining or distance visual acuity and was not associated with any adverse events. While additional clinical evaluation should be conducted to further substantiate the compatibility of Systane Ultra® in this subject group, this clinical study provided evidence of safety and compatibility of Systane® Ultra Lubricant Eye Drops in contact lens wearers.

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## Disclosure

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