



**TRANSMITTED BY FACSIMILE**

Ms. Nancy Yee  
Regulatory Affairs Specialist II  
Santen, Inc.  
555 Gateway Drive  
Napa, CA 94558

RE: **NDA 21-199**  
Quixin (levofloxacin ophthalmic solution), 0.5%  
MACMIS # 11193

Dear Ms. Yee:

This letter objects to Santen, Inc.'s (Santen) dissemination of false or misleading promotional materials for Quixin (levofloxacin ophthalmic solution), 0.5%. As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a promotional flashcard for Quixin (levofloxacin ophthalmic solution), 0.5% identified as QXN-207-00 and entitled, "Antibiotic Susceptibility Pattern of Coagulase-Negative Staphylococci in Patients Undergoing Intraocular Surgery." We have concluded that it is false or misleading in violation of the Federal Food, Drug, and Cosmetic Act (Act) and applicable regulations. Our specific objections follow:

**Background**

Quixin is a sterile ophthalmic solution of levofloxacin, which is a fluoroquinolone antibacterial agent, that is indicated for the treatment of bacterial conjunctivitis, an external or extraocular bacterial infection, caused by susceptible strains of selected organisms.<sup>1</sup>

**Unapproved New Use**

Promotional materials are false or misleading if they contain representations or suggestions that a drug is useful in a broader range of conditions than has been demonstrated by substantial evidence or substantial clinical experience.

Your promotional flashcard features the prominent header on both sides of the card, "Antibiotic Susceptibility Pattern of Coagulase-Negative Staphylococci in Patients Undergoing **Intraocular**

<sup>1</sup> Aerobic gram-positive microorganisms: *Corynebacterium* species, *Staphylococcus aureus* (methicillin-susceptible strains only), *Staphylococcus epidermidis*, (methicillin-susceptible strains only), *Streptococcus pneumoniae*, *Streptococcus* (Groups C/F), *Streptococcus* (Group G), *Viridans* group streptococci; and aerobic gram-negative microorganisms: *Acinetobacter Iwoffii*, *Haemophilus influenzae*, *Serratia marcescens*.

Surgery” (emphasis added) followed by a bar graph entitled, “SUSCEPTIBILITIES & RESISTANCES OF FLUOROQUINOLONES TESTED.” The graph depicts Quixin (levofloxacin) with the highest rate of *in vitro* susceptibility (91%) and the lowest rate of resistance (5%) against coagulase-negative staphylococci compared to norfloxacin, ofloxacin, and ciprofloxacin. In addition, the back of the flashcard states that, “This study suggests that fluoroquinolones and aminoglycosides are effective prophylactic antibiotics against most coagulase-negative staphylococci.” The header and the statement on the back, touting Quixin’s use in intraocular surgery patients, in conjunction with the graph depicting *in vitro* susceptibility and resistance, suggests that Quixin (levofloxacin) is safe and effective to prevent infection caused by coagulase-negative staphylococci in patients undergoing intraocular surgery. This suggestion is false or misleading. Therefore, the flashcard is violative because it suggests that the drug is safe and effective for an unapproved new use, i.e., for prophylactic, preoperative use in intraocular surgery to prevent infections inside the eye.

This claim is particularly troublesome because Quixin has been proven only to be safe and effective in adequate and well-controlled trials for the treatment of bacterial conjunctivitis, an external infection of the delicate membrane that lines the eyelids and covers the exposed surface of the sclera (white) of the eye. FDA is not aware of any substantial evidence or substantial clinical experience that would support Santen's claim that Quixin is safe and effective to prevent internal infections of the eye due to invasive ocular surgery. If, at some future time, you develop such evidence that would support this additional indication, please submit that data in a supplemental NDA to FDA for review.

You should immediately cease dissemination of the promotional flashcard and other similar promotional materials for Quixin that make the same or similar claims or representations. Please respond in writing to us regarding this issue by March 6, 2003. Your response should include Santen’s intent to comply with the above request, the date that you ceased disseminating this promotional flashcard and any other violative promotional materials with the same or similar presentations, and a list of the discontinued materials.

If you have any questions, please contact me by facsimile at (301) 594-6771, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-42; Room 8B-45; 5600 Fishers Lane; Rockville, MD 20857.

We remind you that only written communications are considered official. In all future correspondence regarding this matter, please refer to MACMIS # 11193 and NDA 21-199.

Sincerely,

*{See appended electronic signature page}*

Rebecca Williams, Pharm.D.  
Regulatory Review Officer  
Division of Drug Marketing,  
Advertising, and Communications

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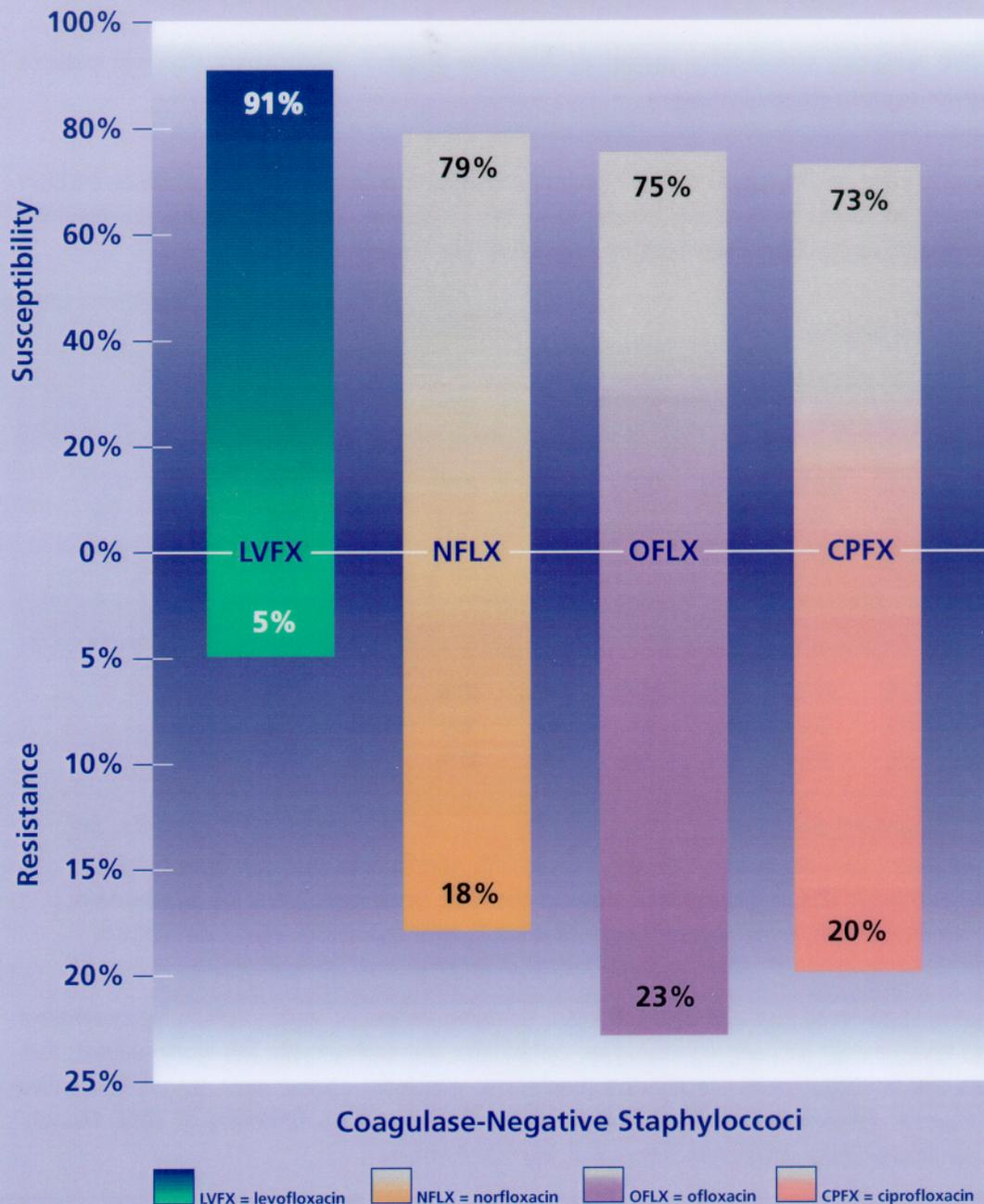
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Rebecca Williams  
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# Antibiotic Susceptibility Pattern of Coagulase-Negative Staphylococci in Patients Undergoing Intraocular Surgery

C.N. Ta, H. Mino de Kaspar, R.T. Chang, E.M. Shriver, P.R. Egbert, K. Singh, M.S. Blumenkranz  
Department of Ophthalmology, Stanford University, Stanford, CA

## SUSCEPTIBILITIES & RESISTANCES OF FLUOROQUINOLONES TESTED



*In vitro* data are not always indicative of clinical success on microbial eradication in a clinical setting.



# Antibiotic Susceptibility Pattern of Coagulase-Negative Staphylococci in Patients Undergoing Intraocular Surgery

C.N. Ta, H. Mino de Kaspar, R.T. Chang, E.M. Shriver, P.R. Egbert, K. Singh, M.S. Blumenkranz  
Department of Ophthalmology, Stanford University, Stanford, CA

## Purpose:

To determine the antibiotic susceptibility pattern of coagulase-negative staphylococci (CNS) in patients undergoing anterior segment intraocular surgery.

## Methods:

Conjunctival cultures were obtained (prior to application of antibiotic or antiseptic agent) from 66 consecutive patients undergoing intraocular surgery who consented to this prospective study. All bacteria isolates were identified and antibiotic susceptibility determined by Kirby-Bauer disc-diffusion technique.

## Results:

A total of 76 CNS were isolated.

ABX	PCN	OX	MET	MZ	CZ	CTX	CAZ	CPX	Levo	NFLX	OFLX
S	12%	55%	60%	34%	79%	87%	20%	73%	91%	79%	75%
I	0%	0%	0%	39%	17%	9%	68%	7%	4%	3%	3%
R	88%	45%	40%	26%	4%	4%	12%	20%	5%	18%	23%
ABX	IPM	MER	Gent	Tobra	Amik	Neo	Eryth	TCN	C	Vanco	
S	97%	93%	97%	95%	97%	71%	49%	71%	79%	100%	
I	0%	4%	0%	0%	0%	20%	4%	15%	0%	0%	
R	3%	3%	3%	5%	3%	9%	47%	15%	21%	0%	

ABX, antibiotic; S, Sensitive; I, Intermediate; R, Resistant; PCN, penicillin; OX, oxacillin; MET, methicillin; MZ, mezlocillin; CZ, cefazolin; CTX, cefotaxime; CAZ, ceftazidime; CPX, ciprofloxacin; Levo, levofloxacin; NFLX, norfloxacin; OFLX, ofloxacin; IPM, imipenem; MER, meropenem; Gent, gentamicin; Tobra, tobramycin; Amik, amikacin; Neo, Neomycin; Eryth, erythromycin; TCN, tetracycline; C, chloramphenicol; Vanco, vancomycin.

## Conclusions:

Coagulase-negative staphylococci isolated from patients undergoing intraocular surgery remain highly sensitive to all antibiotics tested except for penicillin analogues, ceftazidime, and erythromycin. This study suggests that fluoroquinolones and aminoglycosides are effective prophylactic antibiotics against most coagulase-negative staphylococci. Support: Edward E. Hills Fund, Department of Ophthalmology, University of LMU, Munich, Germany, and Hannelore-Georg Zimmerman Foundation, Munich, Germany.

