CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-199

CHEMISTRY REVIEW(S)

SUPPORTING DOCUMENTS:

DMFs:

DMF No.	Holder Name	Subject	Status	Date Reviewed
		Drug substance manufacturer	Inadequate Adequate	H. Khorshidi, HFD-550 3/17/2000 6/20/2000
		Drug product manufacturer/chemical and microbiological testing.	Adequate	H. Khorshidi, HFD-550 6/20/2000. Also refer to this chemistry review
		Alternative microbiological/sterility tester	Adequate	Refer to microbiology review dated 4/14/2000
		Packaging materials- , Eye dropper 5, 11 and 15 ml bottles, plug, Caps	Adequate	H. Khorshidi, HFD-550 6/20/2000
			Adequate	H. Khorshidi, HFD-550 6/20/2000. Also refer to micro-review dated 4/14/2000

RELATED DOCUMENTS (if applicable):

Type	Number	Owner	Subject
IND		Santen	Levofloxacin Ophthalmic solution
NDA	20-634	R.W. Johnson	Levaquin tablets (approval date: 12/20/1996)
NDA	20-635	R.W. Johnson	Levaquin Injection (approval date: 12/20/1996)

CONSULTS:

Consult	Date forwarded	Status	Comments
EER	3/13/2000	OVERALL RESULT: Pending	**Except one site (Winkham laboratories U.K. for microbiological testing), all other sites are acceptable as of 7/19/2000**
Pharmacology, HFD-550	None		
Bio-pharm HFD-550	None		
Statistical analysis, HFD-550	None		

REMARKS/COMMENTS

1. Establishment evaluation requests (EER) has been forwarded on 3/13/2000. Except one site [redacted] all other sites are acceptable by OC.

Overall Result: pending

2. DMF [redacted] originally reviewed and found to be inadequate in support of NDA 21-199 (refer to DMF review dated 3/17/2000).
DMF holder has amended DMF [redacted] on 4/28/2000. The submitted amendment was reviewed and found to be adequate.

3. The first IR letter was send to the applicant on 3/12/2000.
Applicant's response was received on 5/17/2000:
Result: satisfactory (refer to page 10 of this chemistry review).

4. The second IR letter was forwarded to the applicant on 5/2/2000.
Applicant has responded to the second IR letter on 5/12/2000, 5/18/2000 and 5/19/2000 respectively.
Result: satisfactory (refer to pages 40-45 of this chemistry review).

5. The third IR letter was send to the applicant on 6/6/2000.
Applicant has responded on 6/9/2000 and 6/12/2000.
Result: satisfactory (refer to pages 47-52 of this review).

6. The forth and final IR letter was send to the applicant on 6/16/2000.

Applicant has responded on 6/21/2000.
Result: satisfactory (refer to page 52 of this review).

CONCLUSIONS & RECOMMENDATIONS:

From CMC standpoint, This NDA submission is approved pending satisfactory i)- EES results for all manufacturing/testing sites and ii)- response to the labeling comments listed on page 54 of this review. Moreover, comments listed in draft commitments and comments letters of this review (on page 53) should be forwarded to the applicant with the approval letter by the CSO.

cc:
Org. NDA 21-199
HFD-550/Division File
HFD-550/HKhorshidi
HFD-550/LNg
HFD-550/MPuglisi
HFD-550/Wchambers
HFD-830/CwChen

/S/

Hossein S. Khorshidi, Ph.D. Review Chemist

[redacted]

APPEARS THIS WAY
ON ORIGINAL

DIVISION OF Anti-Inflammatory/Analgesics & Ophthalmic Drug products
DAAODP, HFD-550

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-199 **CHEM. REVIEW #** 1 **REVIEW DATE:** 7/19/2000

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	2/28/2000	3/1/2000	3/3/2000
AMENDMENT	5/12/2000	5/16/2000	5/22/2000
AMENDMENT	5/17/2000	5/18/2000	5/24/2000
AMENDMENT	5/18/2000	5/19/2000	5/24/2000
AMENDMENT	5/19/2000	5/23/2000	5/30/2000
AMENDMENT	6/9/2000	6/12/2000	6/14/2000
AMENDMENT	6/12/2000	6/13/2000	6/14/2000
AMENDMENT	6/21/2000	6/22/2000	6/27/2000

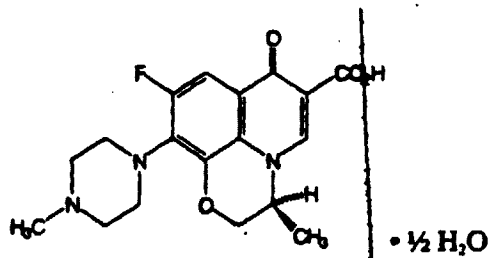
NAME & ADDRESS OF APPLICANT: Santen Inc
555 Gateway Dr
Napa, California 94558

DRUG PRODUCT NAME

Proprietary: Quixin®
Nonproprietary/USAN: Levofloxacin Ophthalmic Solution
Code Name/#:
Chem.Type/Ther.Class: 3P

PHARMACOL. CATEGORY/INDICATION: Anti-bacterial
DOSAGE FORM: Solution
STRENGTHS: 0.5%
ROUTE OF ADMINISTRATION: Topical ocular
DISPENSED: X Rx ___ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



• ½ H_2O

Molecular Formula	$C_{18}H_{20}FN_3O_4$ • ½ H_2O
Molecular Weight	370.38
Stereoisomerism	L-isomer of ofloxacin