CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-023

CHEMISTRY REVIEW(S)

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-023

REVIEW # 4 **DATE REVIEWED:** 12/10/02

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment	12/4/02	12/5/02	12/9/02

NAME & ADDRESS OF APPLICANT:

Allergan Inc.
2525 Dupont Drive
P. O. Box 19534
Irvine, CA 92623

DRUG PRODUCT NAME
Proprietary: RESTASIS
Established: cyclosporine
Code Name/#: 9054x
Chem.Type/Ther.Class: 3p

PHARMACOLOGY CATEGORY: Immunomodulator and anti-inflammatory agent
DOSAGE FORM: Emulsion
STRENGTHS: 0.05%
ROUTE OF ADMINISTRATION: Topical/ocular
DISPENSED: X Rx ___ OTC

PATENT INFORMATION:

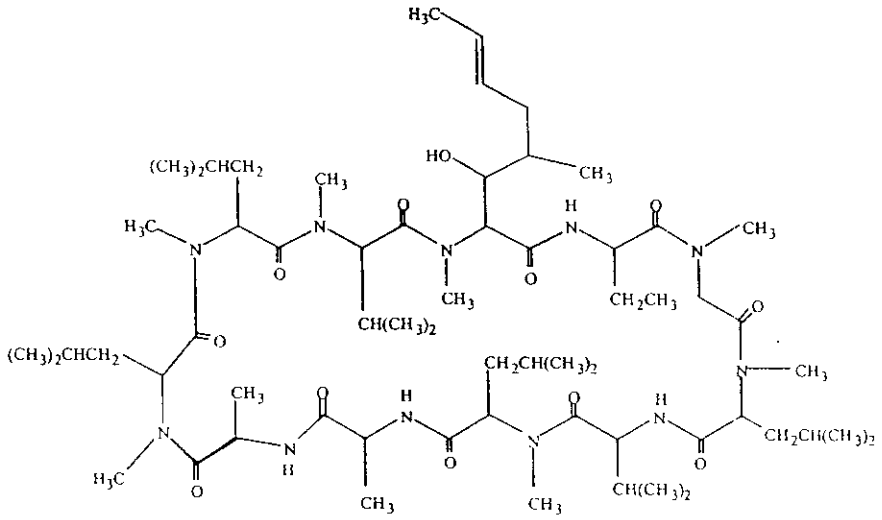
US 4,649,047
US 4,839,342
US 5,474,979

INDICATION: ———

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Molecular Formula
$C_{62}H_{111}N_{11}O_{12}$
Molecular Weight
1202.6

Chemical Name & Structure
Cyclo{[(E)-(2S, 3R, 4R)-3-hydroxy-4-methyl-2-(methylamino)-6-octenoyl]-L-2-aminobutyryl-N-methyglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl}



USAN Name:

Cyclosporine

Allergan Code Number (AGN#)

AGN 192371

Chemical Abstract Number

CAS 059865-13-3

Other Names

Cyclosporine A, cyclosporine, cyclosporin

SUPPORTING DOCUMENTS:

None

REMARKS:

In the chemist's review #3, the application was recommended for approval from chemistry, manufacture, and control standpoint. However due to clinical deficiencies, the NDA was not approved.

In the amendment dated 7/12/99, 7/29/99, and chemist's review # 2, Allergan agreed to monitor impurity [redacted], and [redacted] in the three validation batches, and submitted the results for evaluation, Allergan provides the results of such studies in this amendment.

On Dec. 4, 2002, a teleconference was held with Allergan's representatives discussing the impurities acceptance criteria, an agreement was reached to revise the drug product specification.

CONCLUSIONS & RECOMMENDATIONS:

The application is recommended for approval. All manufacturing facilities are in GMP compliance (as of 10/24/02) The application may be approved for 24 months and — . expiration dates (when stored at 25° C) for the marketed package and respectively.

cc:
Orig. NDA 21-023
HFD-550/Division File
HFD-550/Gorski
HF-550/Chemist/Tso
HFD-830/CChen
HFD-550/Ng
HFD-550/Boyd
HFD-550/Chambers
HFD-550/Mukherjee

Su C. Tso, Ph.D.
Chemist, HFD-550/830

Linda Ng, Ph.D.
Chemistry Team Leader, HFD550

6 Page(s) Withheld

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