CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-184/S-001

Chemistry Review(s)

DIVISION OF DERMATOLOGIC AND DENTAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-184 **CHEM.REVIEW #**: 1 **REVIEW DATE**: 14-SEP-01

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
SE1-001	09-DEC-00	11-DEC-00	11-DEC-00
SE1-001/NC	19-JAN-01	21-JAN-01	21-JAN-01

NAME & ADDRESS OF APPLICANT:

Allergan, Inc.
2525 Dupont Drive
P.O. Box 19534
Irvine, CA 92623-9534

Trudy A. Rumbaugh, MD
Director,
Global Regulatory Affairs
714-246-4292

DRUG PRODUCT NAME:

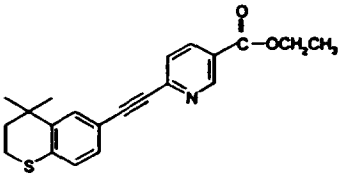
Proprietary:	TAZORAC™ (tazarotene) Cream, 0.05% and 0.1%
Nonproprietary/USAN:	Tazarotene
Code Names/#'s:	AGN190168
Chemical Type:	3
Therapeutic Class:	S

PHARMACOLOGICAL INDICATION: Acne Vulgaris

DOSAGE FORM:	Cream
STRENGTHS:	0.05% and 0.1%
RTE OF ADMINISTRATION:	Topical
DISPENSED:	_x_ R_x ___ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:

NAME:	tazarotene
CHEMICAL NAME:	ethyl 6-[(4,4-dimethylthiochroman-6-yl) ethynyl] nicotinate
CAS NUMBER:	302-79-4
MOL. WT:	351.46
CHEM. FORM:	$C_{21}H_{21}NO_2S$



REMARKS / COMMENTS:

This *clinical efficacy* supplement was submitted to add a second indication to the previously approved drug product NDA 21-184 Tazorac (tazarotene) Cream 0.05% and 0.1%. Note that this NDA covers two different concentrations [in the same dosage form]. The original indication for NDA 21-184 was for once daily treatment of plaque psoriasis. The submission seeks approval for an indication of acne vulgaris.

Only minimal CMC information is necessary to review a clinical efficacy supplement, In particular, a clinical efficacy supplement requires an updated EA and a statement from the sponsor indicating that no CMC changes were made.

Concerning this particular supplement:

This supplement, NDA 21-184 SE1-001 has somewhat of a convoluted history.

A Pre-NDA meeting was held with the sponsor and DDDDP on 11-September 2000. In that meeting, it was agreed that the sponsor could submit a clinical efficacy supplement rather than a new NDA. Regarding CMC, the sponsor wanted to know if:

a) they could cross-reference the API to the previously approved NDA (if, of course, the new submission was to be a NDA). The sponsor was advised in the affirmative.

b) if they could cross-reference the drug product to the previously approved NDA (if, of course, the new submission was to be a NDA). They further stated that they were submitting an updated stability report and an updated EA. They were advised in the affirmative.

NDA 21-184 SE1-001 was received, and CDER-dated, 11 December 2000. Section 4 of the submission was a separate chemistry section containing pages 2-001 through 2-357. In this section was month stability data, a request to increase the stability shelf-life to months, and an updated EA.

The sponsor was notified (via phone) that the shelf-life extension request could not be a part of the efficacy supplement. Submission NDA 21-184 SE1-001/NC withdrew ONLY the CMC (*i.e.*, stability data) portion of SE1-001. In that submission the sponsor agreed to submit the updated stability data in the next annual report.

CMC review of this supplement:

The following CMC data in this supplement is noted and reviewed:

1. The updated EA, which requests a categorical exclusion, is acceptable.

2. The sponsor, in the Pre-NDA meeting, stated that they intended to cross-reference the approved NDA for the API and drug product. Accordingly, the

CMC section of SE1-001 is identical to the CMC section NDA 21-184. This is acceptable.

3. The sponsor owns the manufacturing facility for the API. Manufacturing information for the API was submitted in the NDA (as opposed to a DMF). Hence, there is no DMF to be examined.

There are no labeling issues with this supplement from a CMC perspective.

CONCLUSIONS & RECOMMENDATIONS:

The supplement application is recommended for **Approval** for manufacturing and controls under section 505 of the FFD&C Act.

/S/ 9/24/01

William C. Timmer, Ph.D.
Review Chemist

cc: Orig. NDA 21-184
HFD-540/Division File
HFD-540/Chem/WCTimmer
HFD-540/TmLdr/WHDeCamp
HFD-540/CSO/KBhatt
HFD-540/MO/Hko
HFD-540/PharmTox/ANostrandt