

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-132/S-015

CHEMISTRY REVIEW(S)

**CHEMIST'S REVIEW
OF SUPPLEMENT**

ORGANIZATION:		HFD-120
NDA NUMBER:		20-132
SUPPLEMENT NUMBER:		SCF-015
ORIGINAL SUBMISSION:	Letter Date	Stamp Date
	28-FEB-2003	03-MAR-2003
AMENDMENTS:	Letter Date	Stamp Date
Corrected hyperlinks (C)	14-MAR-2003	17-MAR-2003
Stability update (BC)	16-MAY-2003	19-MAY-2003
Revised stability update (BC)	23-MAY-2003	23-MAY-2003
Response to IR letter (BZ)	20-JUN-2003	23-JUN-2003
RECEIVED BY CHEMIST:		18-MAR-2003

APPLICANT NAME AND ADDRESS: GlaxoSmithKline.
Attn: Mary-Faye Whisler, Ph.D.
Assistant Director, CMC New Submissions (CMC only)
Five Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709

NAME OF DRUG: **IMITREX®**

NONPROPRIETARY NAME: sumatriptan succinate

CHEMICAL NAME / STRUCTURE: 3-[2-(dimethylamino)ethyl-N-methyl-1H-indole-5-methane-sulfonamide succinate (1:1)

DOSAGE FORM(S): Tablets

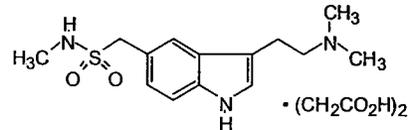
POTENCY(IES): 25 mg, 50 mg and 100 mg

PHARMACOLOGICAL CATEGORY: Migraine

HOW DISPENSED: XX (Rx) (OTC)

RECORDS / REPORTS CURRENT: XX (YES) (NO)

RELATED IND / NDA / DMF(S): NDA 20-080 is cross-referenced for drug substance documentation.



SUPPLEMENT PROVIDES FOR:

The firm proposes reformulation of Imitrex Tablets to allow for a modified mechanism for disintegration and dispersion in the stomach. The submission also provides for revised tablet specifications, which include a new HPLC method for Assay and Related substances and a new Dissolution method.

COMMENTS:

Imitrex (sumatriptan succinate) tablets were approved for treatment of migraine on 01-JUN-1995. In the current supplement, the firm proposes replacing the current immediate release tablet formulation with "fast disintegrating tablet" (FDT) formulation. The new formulations are film-coated oral tablets that are designed to swell and disintegrate rapidly in an acid environment.

The firm is currently targeting March 2004 as the date to initiate replacement of the current products with the FDT formulations. It is estimated that replacement of existing stock will take approximately 4 to 6 weeks for the 50 mg and 100 mg tablets and 8 to 10 weeks for the 25 mg tablets.

The initial submission provided adequate CMC documentation for the composition and manufacture of the proposed formulations. The post-approval stability commitment and expiration dating period were not acceptable, however, and minor deficiencies in analytical procedures and labeling were identified. The deficiencies were communicated to the sponsor on 12-JUN-2003. The firm's 20-JUN-2003 response adequately addresses all CMC concerns.

An acceptable overall compliance recommendation for all proposed manufacturing, packaging and testing sites was received on 03-JUN-2003. [Refer to attached EER.]

CONCLUSIONS AND RECOMMENDATIONS:

Approval of S-015 is recommended.

The *Description* section of the package insert should be checked to verify that the last sentence reads as follows:

Each tablet also contains the inactive ingredients croscarmellose sodium, dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, and sodium bicarbonate.

[The firm has agreed to this revision.]

The action letter should include the standard paragraph regarding cooperation with completion of analytical methods validation.

Martha R. Heimann, Ph.D.

cc: Orig.; NDA 20-132
HFD-120/LChen
HFD-120/MHeimann
HFD-120/MGuzewska/INIT: 6/25/03

Review Completed: June 24, 2003
Filename: C:\DATA\WORD\INDA\N20132\S20132_015.DOC

APPROVED THIS WAY
ON ORIGINAL

22 Page(s) Withheld

§ 552(b)(4) Trade Secret / Confidential

§ 552(b)(4) Draft Labeling

§ 552(b)(5) Deliberative Process

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Martha Heimann
6/25/03 09:57:47 AM
CHEMIST

Maryla Guzewska
6/25/03 10:41:01 AM
CHEMIST

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ON ORIGINAL