CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-308

CHEMISTRY REVIEW(S)

DIVISION OF SPECIAL PATHOGENS AND IMMUNOLOGIC DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-308 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 6/27/01

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE
ORIGINAL	8/31/00	9/1/00
Amendment (BC)	10/26/00	10/27/00

NAME & ADDRESS OF APPLICANT:

Personal Products Company (PPC)
199 Grandview Road
Skillman, New Jersey 08558
Ph# (908) 904-3745

CONTACT:

Barbara Popek, Manager, Regulatory Affairs

DRUG PRODUCT NAME:

Proprietary: Monistat 1 Combination Pack
Established: miconazole nitrate vaginal insert and miconazole nitrate cream
Code #: n/a

PHARMACOLOGICAL CATEGORY/INDICATION:

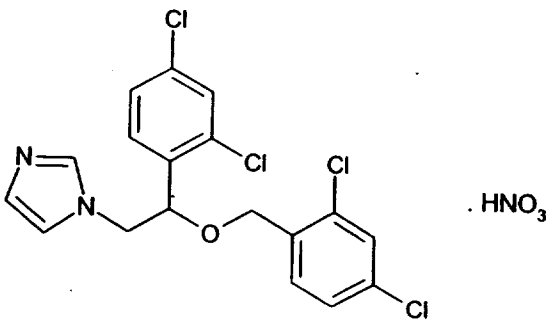
Treatment of vulvovaginal candidiasis.

DOSAGE FORM: Vaginal Insert and External Cream

STRENGTHS: 1200 mg insert and 2% cream
ROUTE OF ADMINISTRATION: Intravaginal and external vulvar

Rx/OTC: Rx
CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Miconazole nitrate, $C_{18}H_{14}Cl_4N_2O.HNO_3$, MW = 479.15
(1) 1*H*-Imidazole, 1-[2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)methoxy]ethyl]-, mononitrate

(2) 1-[2,4-Dichloro-β-[(2,4-dichlorobenzyl)oxy]phenethyl]imidazole mononitrate
CAS 22832-87-7



SUPPORTING DOCUMENTS:

NDA 20-968, [redacted]

RELATED DOCUMENTS:

N/A

CONSULTS:

None

REMARKS/COMMENTS:

This NDA provides for an OTC switch of the Rx product, Monistat Dual-Pak (miconazole nitrate vaginal insert) Soft Gel Vaginal Insert, 1200 mg *and* (miconazole nitrate cream) External Vulvar Cream, 2% that was approved via NDA 20-968 on June 30, 1999 as a one dose treatment for vulvovaginal candidiasis. Since the current application did not include any new CMC information and the reference was made to NDA 20-968, the current review addresses only several CMC issues (see Review Notes for details). The name (both trade and established) of the product was discussed and negotiated with the applicant (for details see the OTC labeling review and the Review Notes of this chemistry review). The source of the gelatin used in the production of the miconazole nitrate vaginal insert was discussed with the [redacted] The detailed information regarding the source of gelatin was submitted to the DMF and was found acceptable. It was confirmed by the DMF holder that the gelatin

used in the manufacture of inserts for the NDA 20-968 (and NDA 21-308) meets the U.S. FDA's September, 1997 Guidance for Industry for "The Sourcing and Processing of Gelatin to Reduce the Potential Risk Posed by Bovine Spongiform Encephalopathy (BSE) in FDA-Regulated Products for Human Use" (gelatin for oral use) and complies with the most recent European BSE related regulations for gelatin. For details see the [redacted] amendments dated April 23 and June 11, 2001.

CONCLUSIONS & RECOMMENDATIONS:

From the chemistry, manufacturing and controls viewpoint, the NDA is recommended for approval.

Dorota Matecka, Ph.D.
Review Chemist, HFD-590

Norman R. Schmuff, Ph.D.
Team Leader, HFD-590

cc: Org. NDA 21-308
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