

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*      **20-827**

**CHEMISTRY REVIEW(S)**

MAR 30 1998

**DIVISION OF SPECIAL PATHOGENS AND IMMUNOLOGIC DRUG  
PRODUCTS**

**Review of Chemistry, Manufacturing, and Controls**

**NDA #:** 20-827

**CHEM.REVIEW #:** 1

**REVIEW DATE:** 30/3/98

<b><u>SUBMISSION/TYPE</u></b>	<b><u>DOCUMENT DATE</u></b>	<b><u>CDER DATE</u></b>
ORIGINAL	3/31/97	3/31/97
Amendment (BZ)	11/18/97	11/19/97
Amendment (BC)	12/4/97	12/5/97
Amendment (BC)	1/29/98	2/5/98
Amendment (BC)	2/19/98	2/20/98
Amendment (BC)	3/6/98	?

**NAME & ADDRESS OF APPLICANT:**

Advanced Care Products  
P.O. Box 6024  
691 U.S. Route 1 South  
North Brunswick, New Jersey 08902  
Ph# (908) 524-1675

**CONTACT:**

Diane Herron, Director, Regulatory Affairs

**DRUG PRODUCT NAME:**

**Proprietary:** Monistat 3 Vaginal Cream  
**Established:** Miconazole Nitrate, USP  
**Code #:** n/a

**PHARMACOLOGICAL CATEGORY/INDICATION:**

Treatment of vulvovaginal candidiasis.

**DOSAGE FORM:** Vaginal Cream

**STRENGTHS:** 4% cream, 200 mg per applicator

**ROUTE OF ADMINISTRATION:** Intravaginal

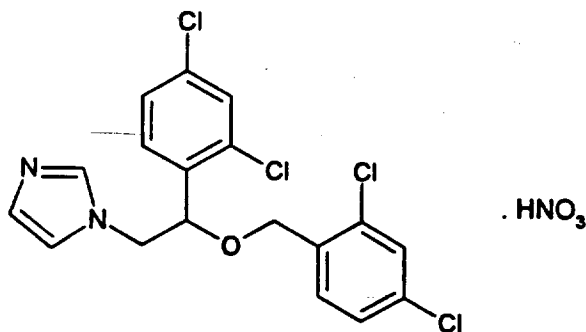
**Rx/OTC:** OTC

**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- $\beta$ -[(2,4-dichlorobenzyl)oxy]phenethyl]imidazole mononitrate  
CAS 22832-87-7



**SUPPORTING DOCUMENTS:**

**CONSULTS:**

Trademark review (complete 9/9/97, satisfactory).

Site inspection (complete 2/6/98, satisfactory).

Environmental Assessment (categorical exclusion request acceptable).

**REMARKS/COMMENTS:**

Monistat 3 Vaginal Cream is a modified, patented formula (AV.03.02.0077) of miconazole nitrate vaginal cream, in which drug substance is suspended in the emulsion (oil in water). CMC details regarding the drug substance are contained in the DMF [redacted] (miconazole nitrate, drug substance [redacted]) and DMF [redacted] (Intermediate [redacted]) and are not repeated in this submission. Deficiencies, which found in both DMFs were of a minor nature and were addressed by their holder [redacted] adequately. The base cream

formula is equivalent to the Miconazole Nitrate (2.0 %) New Base Vaginal Cream (Monistat 7 Vaginal Cream), product recently approved by the FDA in the supplement SCF-043 to the approved NDA 17-450.

**CONCLUSIONS & RECOMMENDATIONS:**

The NDA submission and amendments provide adequate information on the chemistry, manufacturing and controls for the production of Monistat 3 Vaginal Cream. The related GMP and product specific inspections of the manufacturing facilities have been completed and found satisfactory. From the chemistry, manufacturing and controls viewpoint, the NDA is recommended for approval.

/S/

3/30/98

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

/S/

3/30/98

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

cc: Org. NDA 20-827  
HFD-590/Division File  
HFD-590/Team Leader/NSchmuff  
HFD-830/DivDir/CChen  
HFD-590/Chem/DMatecka  
HFD-590/MO/DDavies  
HFD-590/Pharm/OMcMaster  
HFD-590/Micro/LGoosey  
HFD-590/CSO/CChin  
District Office