CENTRAL FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
ANDA 76-837

Name: Fluconazole Injection, 2 mg/mL
(in 0.9% Sodium Chloride Injection)

Packaged in 200 mg/100 mL and
400 mg/200 mL single-dose flexible
plastic containers

Sponsor: SICOR Pharmaceuticals, Inc.

Approval Date: January 13, 2005
APPLICATION NUMBER:
ANDA 76-837

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 76-837

APPROVAL LETTER
SICOR Pharmaceuticals, Inc.  
Attention: Rosalie A. Lowe  
19 Hughes  
Irvine, CA 92618-1902

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated August 29, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Fluconazole Injection, 2 mg/mL, (in 0.9% Sodium Chloride Injection), packaged in 200 mg/100 mL and 400 mg/200 mL single-dose flexible plastic containers.

Reference is also made to your amendments dated July 14, August 17, August 27, October 19, and December 3, 2004.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Fluconazole Injection, 2 mg/mL (in 0.9% Sodium Chloride Injection) to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Diflucan® Injection, 2 mg/mL (in 0.9% Sodium Chloride) of Pfizer Central Research).

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed
launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising, and Communications, HFD-42
5600 Fishers Lane
Rockville, MD 20857

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications (HFD-42) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

Gary Buehler 1/13/05
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
cc: ANDA 76-837
Division File
Field Copy
HFD-610/R. West
HFD-205
HFD-610/Orange Book Staff

Approved Electronic Labeling Located at: xxxxxxx

Endorsements:
HFD-640/Z. Getahun/ 12/23/04
HFD-643/R. Adams/ 2/23/05
HFD-617/T. Palat/12/20/04
HFD-613/C. Park/ 12/27/04
HFD-613/L. Golson/ 1/3/05

V:\FIRMSNZ\SICOR\LTRS&REV\76837.AP.DOC

F/T by rad12/22/04

APPROVAL
APPLICATION NUMBER:
ANDA 76-837

LABELING
4 weeks after the end of treatment the percentages of patients with clinical relapse
creatinine clearance. The dose of fluconazole may need to be reduced in patients with
clearance decreased 45% ± 15% (range: -15 to -60%). (See
administered to 13 normal male volunteers following oral fluconazole 200 mg
time to a mean of 53.2 hours six days later and 46.6 hours 12 days later.
In premature newborns (gestational age 26 to 29 weeks), the mean (%cv) clearance
the plasma concentration-time curve) are dose proportional.
effect in systemic infection with
leads to a mean Cmax of 6.72 mcg/mL (range: 4.12 to 8.08 mcg/mL) and after single
mean ± SD increase in fluconazole AUC and Cmax of 45% ± 31% (range: 19 to 114%)
and 43% ± 31% (range: 19 to 122%), respectively. These changes are attributed to a
elimination of fluconazole.
Warfarin:
There was a significant increase in prothrombin time response (area under
response to oral anticoagulation with warfarin of 8.5% ± 10.5% (range: 2.4 to 24.3%) at
sensitivity to fluconazole
There have been reports of cases of superinfection with
PRECAUTIONS.
The effects of fluconazole on the pharmacokinetics of the
300 mg to 21 normal females taking an oral contraceptive containing ethinyl estradiol
were statistically significantly different from placebo. Fluconazole treatment did not cause a
increase in phenytoin AUC was 88% ± 68% (range: 16 to 247%). The absolute
administration of fluconazole 200 mg daily for 14 days in eight renal transplant
9 months– Single-Oral 0.51 (60%) 19.5 9.8 (20%) —
13 years 2 mg/kg N=14 N=16
9 months– Single-Oral 0.40 (38%) 25.0 2.9 (22%) —
In children, the following pharmacokinetic data {Mean(%cv)} have been reported:
9 months– Single-Oral 0.34 (31%) 19.8 4.1 (51%) —
Normal skin 10
There have been published reports that an interaction exists when
sensitivity to fluconazole
There have been reports of cases of superinfection with
PRECAUTIONS.
The effects of fluconazole on the pharmacokinetics of the
1 day to 6 months have been treated safely with fluconazole.

Creatinine clearance in adults:

Premature newborns. (See

Interactions may occur.

Found that concomitant fluconazole 200 mg once daily and cisapride 20 mg four times plasma concentration of these agents. When fluconazole is used concomitantly with treatment should be administered for at least 2 weeks to decrease the likelihood of resolution of symptoms.

The use of fluconazole in children with cryptococcal meningitis, systemic candida infections:

Indicate that active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection. Patients with AIDS and cryptococcal

In Phase II/III clinical trials conducted in the United States and in Europe, 577 pediatric patients were similar. The proportions of patients discontinuing (See

Fluconazole is primarily cleared by renal excretion as unchanged drug. Because elderly factors, such as structural heart disease, electrolyte abnormalities and concomitant proarrhythmic conditions.

Because of the voluntary nature of the reports and the natural increase in the incidence spontaneous reports of anemia and acute renal failure were more frequent among patients with esophageal candidiasis.

Casual relationship to drug exposure.

Creatinine clearance is recommended in patients receiving transplant patients with or without renal impairment. Careful monitoring of

Tacrolimus:

Cyclosporine concentrations and serum creatinine is recommended in patients receiving

Rifabutin:

Rifampin:

Phenytoin

Coumarin-type anticoagulants:

Coumarin-type anticoagulants may be associated with elevations

Midazolam:

Depending on clinical circumstances, consideration should be given to increasing the

Drug Interaction Studies.

Drugs that interfere with the production of vitamin D should also be discontinued. Drugs metabolized by the cytochrome P450 system may be associated with elevations

Probenecid:

Cimetidine:

Methadone:

Valproic acid:

Fluconazole may significantly increase cyclosporine levels in renal

Fluconazole may also cause a small increase in cyclosporine levels in nonrenal transplant

Cyclosporine:

Cyclosporine concentrations and serum creatinine is recommended in patients receiving

CONTRAINDICATIONS

Do not use fluconazole in patients with known hypersensitivity to fluconazole or other azole antifungals.

Pregnancy

Teratogenic effects. Pregnancy Category C:

Pregnancy

Oral sulfonylurea hypoglycemic agents added to metformin therapy. In order to monitor both drugs in a safe manner, it is advisable to discontinue metformin therapy or

Seizures, dizziness.

The use of fluconazole in nursing mothers is not recommended.

The potential benefits of fluconazole for the foetus must be carefully weighed against the potential risk to the mother.

The potential benefit justifies the possible risk to the fetus.

In addition, the following adverse events have occurred during post-marketing

Severe gastrointestinal effects, including gastrointestinal bleeding, have been

Severe or life-threatening dermatologic effects have occurred rarely with fluconazole.

Exfoliative skin disorders including Stevens-Johnson syndrome and

Abdominal pain 2.8 1.6

Creatinine Clearance (mL/min) Percent of Recommended Dose

Regular dialysis 100% after each dialysis

>50 100%

50 (no dialysis) 50%

>10 100%

<10 100%

(N=577) (N=451)

29% 37%

29% 37%

(N=577) (N=451)

Cyclosporine concentrations and serum creatinine is recommended in patients receiving

Cyclosporine:

Cyclosporine concentrations and serum creatinine is recommended in patients receiving
Fluconazole Injection
Iso-Osmotic SODIUM CHLORIDE Diluent

200 mg (2 mg/mL)

Each 100 ml contains 200 mg of fluconazole and 900 mg of sodium chloride, USP in water for injection, USP.

Osmolarity is 315 mOsmol/L (calc).

Usual Dosage: See Package Insert.

CAUTIONS: Do not add supplementary medication. Must not be used in series connections. Do not use unless solution is clear.

STORAGE: STORE UNITS IN OVERWRAP BETWEEN 5°C TO 25°C (41°F TO 77°F) UNTIL READY TO USE. AVOID EXCESSIVE HEAT. PROTECT FROM FREEZING.

sicor™
SICOR Pharmaceuticals, Inc.
Irvine, CA 92618

APPROVED

JAN 13 2005
200 mL

NDC 0703-1020-31

**Fluconazole Injection**
Iso-Osmotic SODIUM CHLORIDE Diluent

400 mg (2 mg/mL)

Single Dose Container
Sterile Nonpyrogenic
FOR INTRAVENOUS INFUSION ONLY

sicor™
SICOR Pharmaceuticals, Inc.
Irvine, CA 92618

104001

Each 200 mL contains: 400 mg of fluconazole and 1.8 g of sodium chloride, USP in water for injection, USP.

Osmolarity is 315 mOsmol/L (calc).

**Usual Dosage:** See Package Insert.

**CAUTIONS:** Do not add supplementary medication. Must not be used in series connections. Do not use unless solution is clear.

**STORAGE:** STORE UNITS IN OVERWRAP BETWEEN 5°C TO 25°C (41°F TO 77°F) UNTIL READY TO USE. AVOID EXCESSIVE HEAT. PROTECT FROM FREEZING.

APPROVED

JAN 13 2015
SICOR Pharmaceuticals, Inc.

FLUCONAZOLE INJECTION
ANDA 76-837

Response to Deficiency Letter of July 14, 2004

SHELFPACK LABEL
200 mg

CAUTIONS: Squeeze and inspect inner container which maintains product sterility. Discard if leaks are found. Do not add supplementary medication. Must not be used in series connections. Do not use unless solution is clear.

STORAGE: STORE UNITS IN OVERWRAP BETWEEN 5° TO 25°C (41° TO 77°F) UNTIL READY TO USE. AVOID EXCESSIVE HEAT.

PROTECT FROM FREEZING.

NDC 0703-1029-30 13only

1 Each 100 mL contains 200 mg of fluconazole and 900 mg of sodium chloride, USP in water for injection, USP.

Osmolarity is 315 mOsm/L (calc).

Usual Dosage: See Package Insert.

Approved
JAN 13 2005

Sterile Nonpyrogenic
6 Single-dose plastic containers x 100 mL
SHELFPACK LABEL
400 mg

CAUTIONS: Squeeze and inspect inner container which maintains product sterility. Discard if leaks are found. Do not add supplementary medication. Must not be used in series connections. Do not use unless solution is clear.

STORAGE: STORE UNITS IN OVERWRAP BETWEEN 5° TO 25°C (41° TO 77°F) UNTIL READY TO USE. AVOID EXCESSIVE HEAT, PROTECT FROM FREEZING.

sicor™
SICOR Pharmaceuticals, Inc.
Irvine, CA 92618

Fluconazole Injection
Iso-Osmotic SODIUM CHLORIDE Diluent

400 mg
(2 mg/mL)

Sterile Nonpyrogenic
6 Single-dose plastic containers x 200 mL

Each 200 mL contains 400 mg of fluconazole and 1.8 g of sodium chloride, USP in water for injection, USP.
Osmolarity is 315 mOsm/L (calc).
Usual Dosage: See Package Insert.

APPROVED
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 76-837

LABELING REVIEWS
ANDA Number: 76-837          Date of Submission: August 29, 2003

Applicant's Name: Sicor Pharmaceuticals, Inc.

Established Name: Fluconazole Injection, 2 mg/mL (in 0.9% Sodium Chloride Injection)

1. GENERAL

Delete the term ——— in association with "Plastic Container" from the labels and labeling.

2. CONTAINER - 200 mg/100 mL & 400 mg/200 mL

   a. We encourage you to differentiate your drug product strengths (200 mg & 400 mg) by using boxing, contrasting colors, and/or some other means.

   b. Include the total volume (i.e., 100 ml or 200 mL), preferably at the upper left corner of the container labels.

   c. Include the text "FOR INTRAVENOUS INFUSION ONLY", preferably beneath the text "Sterile Nonpyrogenic".

   d. Revise to read "CAUTIONS: ..." [plural]

   e. Increase the prominence of the term "Rx Only".

   f. Revise your storage temperature statement to be the same as the one proposed for your Shelf Pack Label.

   g. We note that you included information regarding your unapproved drug product in glass vial (ANDA 76-653) throughout the insert labeling. Please note that ANDA 76-653 must be approved prior to the approval of this application or these applications must be approved at the same time. Otherwise, further revisions will be necessary prior to approval of this application.

3. OVERWRAP

We note that you did not submit overwrap labeling. Please submit and/or comment.

4. SHELF PACK CARTON

   a. See comments 1(d) & 1(g) above.

   b. Revise the net quantity statement to read "6 Single-dose plastic containers x 100 mL (or 200 mL)".

5. INSERT

   a. General

   Delete the term ——— in association with "plastic containers" throughout the insert labeling.

   b. TITLE

   We encourage the Inclusion of the text "For Intravenous Infusion Only" beneath the established name.
c. DESCRIPTION

i. Second paragraph:

"molecular formula" rather than ______ formula"

ii. Include information specific to your proposed plastic container as the last paragraph and/or comment. We refer you to the innovator's labeling in this regard.

d. CLINICAL PHARMACOLOGYY - Pharmacokinetics and Metabolism

Delete the last sentence of the first paragraph.

e. ADVERSE REACTIONS - In Patients Receiving Multiple Doses for other infections:

Revise this subsection heading to read "In Patients Receiving Multiple Doses for Other Than Vaginal Candidiasis".

f. DOSAGE AND ADMINISTRATION (Second paragraph, first sentence) - Revise to read:

The daily dose of fluconazole for the treatment of infections other than vaginal candidiasis should be...

g. HOW SUPPLIED

i. First sentence - Revise to read:

...as sterile solution in iso-osmotic Sodium Chloride Diluent containing...

ii. See comment 1(g) above.

iii. ...mL glass vial packaged... [add "glass"]

iv. ...mL plastic container packaged... ["plastic container" rather than ____]

v. Revise "______" to read "200 mL"

vi. Revise to read "Glass Vial Storage." [add "Glass"]

vii. Revise to read "Plastic Container Storage." [delete ____]

Please revise your labels and labeling, as instructed above, and submit in final print, or in draft if you prefer.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

http://www.fda.gov/cder/cdernew/listserv.html
To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

[Signature]

William Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL
FOR THE RECORD:

1. MODEL LABELING – Diflucan Injection (NDA 19-950/S-028) labeling approved on Feb 22 1999. The innovator has a combined package insert labeling for injection, tablets and powder for oral suspension. S-034 approved 8/7/02 is specifically related to the approval of PPI for the 150 mg tablets.

2. This drug product is not the subject of a USP monograph

3. The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 1054 (Volume 1.1).

4. Patent Data

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Exclusivity Data
There is no unexpired exclusivity for this product.

The sponsor has filed Patent Certification III.

5. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Plastic container - RLD - Store between 77°F (25°C) and 41°F (5°C). Brief exposure up to 104°F (40°C) does not adversely affect this product. Protect from freezing. Avoid excessive heat.

ANDA: Same as the RLD.

Glass vial - Both RLD and the ANDA: Store between 50 to 30°C (41°C to 86°F). Protect from freezing.

6. PACKAGING CONFIGURATIONS

RLD: 200 mg/100 mL & 200 mg/200 mL (in glass & Plastic; in Sodium Chloride & Dextrose)
ANDA – 200 mg/100 mL & 200 mg/200 mL (in both plastic container and glass vial in Sodium Chloride) However, see comment 1(g) above.

7. CONTAINER/CLOSURE - The following is from the chemist's review. There is no information submitted on the glass vial.

The summary of Container Closure System (CCS) for Fluconazole Infusion bags for Lot #s: X03C501 and X03C501F1 (100 mL and 200 mL Fill Bags):

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>Certificate of Compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Container</td>
<td>MC312 Infusion bag 100 mL bag/ 250 mL bag Cryovac Sealed Corp.</td>
<td>p. 2025</td>
</tr>
<tr>
<td>Port</td>
<td></td>
<td>p. 2121</td>
</tr>
</tbody>
</table>
The results for USP systemic toxicity study for the CCS are on pp. 2026 – 2046. The USP <661> test results are on pp. 2049 -2052. The container meets the JPXIII test for resistance to water vapor permeation. (p. 2055).

The Certificate of Compliance for the Spike Ports and for the Connector Tubing state that the extracts from each meet the requirements of a USP Plastic Class VI. The details of the biological, physicochemical and toxicology tests methods and results are provided (pp. 2122 – 2159, pp. 2162 - 2190).

8. The following was determined at the time of ANDA 76-087 in the past.

The innovator has a combined package insert labeling for fluconazole tablet, oral solution and injection. The Pharmacokinetics and Metabolism of the CLINICAL PHARMACOLOGY section reads “The pharmacokinetic properties of fluconazole are similar following administration by the intravenous or oral routes. In normal volunteers, the bioavailability of orally administered fluconazole is over 90% compared with intravenous administration.” Also, the D&A section reads that “Since oral absorption is rapid and almost complete, the daily dose of fluconazole is the same for oral and intravenous administration. The majority of the information in this section is associated with the oral regimen. For these reasons, we will allow the generic sponsor retain all information for oral regimen. However, a single oral dose of fluconazole 150 mg is specifically for “Vaginal Candidiasis” only. Therefore, we will have the generic sponsors silent on all information specifically associated with “Vaginal Candidiasis”

9. The proposed labeling does not contain any information specifically associated with “Vaginal Candidiasis” throughout the text. This indication is specifically associated with Single administration of Diflucan tablet, 150 mg.

10. The following e-mail was sent to PM in the new drug division on 1/24/02 and answer form the division on 1/29/02. (See file folder for detail)

Question:

The combined insert for the oral tablet, suspension & injection contains indications for Oropharyngeal and Esophageal candidiasis. We have a generic application for the injection only. Would you please let us know that fluconazole injection is also indicated for these symptoms. If only oral suspension is indicated for the treatment of these, then we have to direct the generic sponsor to carve out the information associated with these from the insert labeling. Your help would be appreciated. Thanks,

Chan

Answer:

As far as I can tell all three formulations are indicated for OPC and EC. I am not aware of any reasons barring applicants from applying separately for those indications using each formulation.

Imo (Ibia, Ekopino)

11. The review for the container labels and overwrap was done using RLD labeling for the same packaging configuration. It appears that the RLD labeling for the glass bottle and plastic bags are not identical to each other.

12. This drug product is manufactured by Sicor Pharmaceutical, Inc. (p.1103, vol.1.2)
cc:
ANDA: 76-837
DUP/DIVISION FILE
HFD-613/Cpark/LGolson (no cc)
V:\FIRMS\NZ\SICOR\LTRS\REV\76837\na1LABELING.doc
Review

APPEARS THIS WAY
ON ORIGINAL
ANDA Number: 76-837  Date of Submission: July 14, 2004

Applicant's Name: Sicor Pharmaceuticals, Inc.

Established Name: Fluconazole Injection, 2 mg/mL (in 0.9% Sodium Chloride Injection)

1. **GENERAL**

   We note that you included information regarding your unapproved drug product in a glass vial (ANDA 76-653) throughout the insert labeling. Please note that ANDA 76-653 must be approved prior to the approval of this application or these applications must be approved at the same time. Otherwise, further revisions will be necessary prior to approval of this application.

2. **CONTAINER - 200 mg/100 mL & 400 mg/200 mL**

   Add the statement "Protect from freezing." to the storage temperature statement and/or comment.

3. **OVERWRAP**

   We acknowledge that you will employee clear overwrap without text. Please verify that your proposed overwrap is sufficiently clear so that all text appearing on the containers is sufficiently legible through the overwrap. Please comment.

4. **INSERT**

   a. **DESCRIPTION:**

      As discussed between Chan Park of the Agency and Sonya Hernandez of your firm via a tele-conference on July 20, 2004, the following statement specific to your container system should be found acceptable based on your response to the chemistry deficiencies regarding this issue. We defer the comment pending review of your chemistry response.

      *The plastic container is composed of sterilizable medical grade film. (Cryovac M312 Pharmaceutical Solution Film). The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period. However, the suitability of the plastic has been confirmed in tests in animals according to USP biological tests for plastic containers as well as by tissue culture toxicity studies.*

   b. **HOW SUPPLIED**

      See GENERAL COMMENT above.

Please revise your labels and labeling, as instructed above. Please note that the electronic labeling rule published December 11, 2003, (88 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. (Refer to Final Rule [Docket No. 2000N-1652] http://www.fda.gov/OHRMS/DOCKETS/98fr/03-30641.htm). To assist in our review, we request that labeling also be submitted in MS Word format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -
http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

[Signature]

William Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL
QUESTIONS/NOTES TO THE CHEMIST - The following e-mail was sent to the chemist on 7/20/04. Also refer to the comment under insert above.

Hi Zelleka,

Please do me a favor. The sponsor included the following language in the insert labeling regarding their container. I was informed that they do not have other approved applications which used the same packaging and the same language in the labeling. Please review the language to see this is accurate and acceptable in terms of chemistry view point. Thank you for your help,

Chan

The plastic container is composed of sterilizable medical grade film. (Cryovac M312 Pharmaceutical Solution Film). The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period. However, the suitability of the plastic has been confirmed in tests in animals according to USP biological tests for plastic containers as well as by tissue culture toxicity studies.

FOR THE RECORD:

1. MODEL LABELING – Diflucan Injection (NDA 19-950/S-028) labeling approved on Feb 22 1999. The innovator has a combined package insert labeling for injection, tablets and powder for oral suspension. S-039 approved 3/24/04 is specifically related to the approval of revised PPI for the 150 mg tablets.

2. This drug product is not the subject of a USP monograph.

3. SHELF PACK CARTON - Satisfactory in FPL as of 7/14/04 submission (vol. 2.1)

4. The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 1054 (Volume1.1).

5. Patent Data

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Exclusivity Data

There is no unexpired exclusivity for this product.

The sponsor has filed Patent Certification III.

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Plastic container - RLD - Store between 77°F (25°C) and 41°F (5°C). Brief exposure up to 104°F (40°C) does not adversely affect this product. Protect from freezing. Avoid excessive heat.

ANDA: Same as the RLD.

Glass vial - Both RLD and the ANDA: Store between 50 to 300°C (410 to 86°F). Protect from freezing.
7. PACKAGING CONFIGURATIONS

RLD: 200 mg/100 mL & 200 mg/200 mL (in glass & Plastic; in Sodium Chloride & Dextrose)
ANDA – 200 mg/100 mL & 200 mg/200 mL (in both plastic container and glass vial in Sodium Chloride) However, see GENERAL COMMENT above.

8. CONTAINER/CLOSURE - The following is from the chemist's review. There is no information submitted on the glass vial.

The summary of Container Closure System (CCS) for Fluconazole Infusion bags for Lot #s: X03C501 and X03C501F1 (100 mL and 200 mL Fill Bags):

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<tr>
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<td></td>
<td>p. 2121</td>
</tr>
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<td>--- Connector Tubing</td>
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<td></td>
</tr>
<tr>
<td>Over wrap</td>
<td>This is secondary packaging; it is not intended to be a sterility or moisture barrier</td>
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The results for USP systemic toxicity study for the CCS are on pp. 2026 – 2046. The USP <661> test results are on pp. 2049 -2052. The container meets the JPXIII test for resistance to water vapor permeation. (p. 2055).

The Certificate of Compliance for the Spike Ports and for the Connector Tubing state that the extracts from each meet the requirements of a USP Plastic Class VI. The details of the biological, physicochemical and toxicology tests methods and results are provided (pp. 2122 – 2159, pp. 2162 - 2190).

9. The following was determined at the time of ANDA 76-087 in the past.

The innovator has a combined package insert labeling for fluconazole tablet, oral solution and injection. The Pharmacokinetics and Metabolism of the CLINICAL PHARMACOLOGY section reads “The pharmacokinetic properties of fluconazole are similar following administration by the intravenous or oral routes. In normal volunteers, the bioavailability of orally administered fluconazole is over 90% compared with intravenous administration.” Also, the D&A section reads that “Since oral absorption is rapid and almost complete, the daily dose of fluconazole is the same for oral and intravenous administration. The majority of the information in this section is associated with the oral regimen. For these reasons, we will allow the generic sponsor retain all information for oral regimen. However, a single oral dose of fluconazole 150 mg is specifically for “Vaginal Candidiasis” only. Therefore, we will have the generic sponsors silent on all information specifically associated with “Vaginal Candidiasis”

10. The proposed labeling does not contain any information specifically associated with "Vaginal Candidiasis" throughout the text. This indication is specifically associated with Single administration of Diflucan tablet, 150 mg.

11. The following e-mail was sent to PM in the new drug division on 1/24/02 and answer form the division on 1/29/02. (See file folder for detail)

Question:

The combined insert for the oral tablet, suspension & injection contains indications for Oropharyngeal and Esophageal candidiasis. We have a generic application for the injection only. Would you please let us know that fluconazole injection is also indicated for these symptoms. If only oral suspension is indicated for the treatment of these, then we
have to direct the generic sponsor to carve out the information associated with these from the insert labeling. Your help would be appreciated. Thanks,

Chan

Answer:

As far as I can tell all three formulations are indicated for OPC and EC. I am not aware of any reasons barring applicants from applying separately for those indications using each formulation.

Imo (Ibia, Ekopino)

11. The review for the container labels and overwrap was done using RLD labeling for the same packaging configuration. It appears that the RLD labeling for the glass bottle and plastic bags are not identical to each other.

12. This drug product is manufactured by Sicor Pharmaceutical, Inc. (p.1103, vol.1.2)

Date of Review: 7/20/04
Date of Submission: 7/14/04

Primary Reviewer: Chan Park

Team Leader: [Signature] Date: 7/28/04

Team Leader: [Signature] Date: 7/30/04

cc:
ANDA: 76-837
DUP/DIVISION FILE
HFD-613/Cpark/LGolson (no cc)
V:\FIRMSNZ\SICOR\LTRS&REV\76837na2.LABELING.doc
Review

APPEARS THIS WAY ON ORIGINAL
ANADA Number: 76-837  Date of Submission: August 27, 2004

Applicant's Name: Sicon Pharmaceuticals, Inc.

Established Name: Fluconazole Injection, 2 mg/mL (in 0.9% Sodium Chloride Injection)

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

CONTAINER LABELS - 200 mg/100 mL & 400 mg/200 mL
Satisfactory in FPL as of 8/27/04 submission (vol. 3.1)

SHELFPACK LABEL - 6 x 100 mL or 6 x 200 mL
Satisfactory in FPL as of 8/27/04 submission (vol. 3.1)

OVERWRAP POUCH
The sponsor proposed a clear pouch. Pouch is clear enough so that the text on the labels is sufficiently legible per the sponsor's statement submitted 8/27/04.

PROFESSIONAL PACKAGE INSERT LABELING
Satisfactory in FPL as of 8/27/04 submission (vol. 3.1, Rev. March 2004)

BASIS OF APPROVAL:
Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Diflucan® Injection

NDA Number: 19-950

NDA Drug Name: Diflucan® Injection

NDA Firm: Pfizer, Inc.

Date of Approval of NDA Insert and supplement #:
PI - 19-950/S-028, approved February 22, 1999
PPI - 19-950/S-039 approved 3/24/04 is specifically related to the approval of revised PPI for the 150 mg tablets.

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance? No
QUESTIONS/NOTES TO THE CHEMIST - The following e-mail was to/from the chemist on the packaging material.

Question - Hi Zelleka,

Please do me a favor. The sponsor included the following language in the insert labeling regarding their container. I was informed that they do not have other approved applications which used the same packaging and the same language in the labeling. Please review the language to see this is accurate and acceptable in terms of chemistry view point. Thank you for your help, Chan

The plastic container is composed of sterilizable medical grade film. (Cryovac M312 Pharmaceutical Solution Film). The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period. However, the suitability of the plastic has been confirmed in tests in animals according to USP biological tests for plastic containers as well as by tissue culture toxicity studies.

Answer from the chemist:

I read the statement that you e-mailed, and I think that it is fine, as long as the RLD also uses the same Cryovac M312 Pharmaceutical Solution Film. I have seen such a statement on an innovator's label. Although the statement is vague and does not spell out exactly how much water or what chemicals leach out of the container. I believe if something is good enough for the RLD it is fine for the ANDA.

Please let me know if I may be of further help.
Zelleka

FOR THE RECORD:

1. MODEL LABELING – Diflucan Injection (NDA 19-950/S-028) labeling approved on Feb 22 1999. The innovator has a combined package insert labeling for injection, tablets and powder for oral suspension. S-039 approved 3/24/04 is specifically related to the approval of revised PPI for the 150 mg tablets.

2. The sponsor proposed a combined package insert labeling with ANDA 76-653 (Fluconazole injection in glass vial). 76-653 has been approved on July 29, 2004.

3. Pertaining the description of plastic container used for this drug product, please refer to the answer from the chemist above. The sponsor’s description appears accurate per the chemist.

4. This drug product is not the subject of a USP monograph.

5. The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 1054 (Volume 1).

6. Patent Data/Exclusivities
   None

7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

   Plastic container - RLD - Store between 77°F (25°C) and 41°F (5°C). Brief exposure up to 104°F (40°C) does not adversely affect this product. Protect from freezing. Avoid excessive heat.

   ANDA: Same as the RLD.

   Glass vial - Both RLD and the ANDA: Store between 50 to 30°C (410 to 86°F). Protect from
freezing.

8. PACKAGING CONFIGURATIONS

RLD: 200 mg/100 mL & 200 mg/200 mL (in glass & Plastic; in Sodium Chloride & Dextrose)
ANDA – 200 mg/100 mL & 200 mg/200 mL (in both plastic container and glass vial in Sodium Chloride)

9. CONTAINER/CLOSURE - The following is from the chemist's review.

The summary of Container Closure System (CCS) for Fluconazole Infusion bags for Lot #s: X03C501 and X03C501F1 (100 mL and 200 mL Fill Bags):

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The innovator has a combined package insert labeling for fluconazole tablet, oral solution and injection. The Pharmacokinetics and Metabolism of the CLINICAL PHARMACOLOGY section reads "The pharmacokinetic properties of fluconazole are similar following administration by the intravenous or oral routes. In normal volunteers, the bioavailability of orally administered fluconazole is over 90% compared with intravenous administration." Also, the D&A section reads that "Since oral absorption is rapid and almost complete, the daily dose of fluconazole is the same for oral and intravenous administration. The majority of the information in this section is associated with the oral regimen. For these reasons, we will allow the generic sponsor retain all information for oral regimen. However, a single oral dose of fluconazole 150 mg is specifically for "Vaginal Candidiasis" only. Therefore, we will have the generic sponsors silent on all information specifically associated with "Vaginal Candidiasis"

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The combined insert for the oral tablet, suspension & injection contains indications for Oropharyngeal and Esophageal candidiasis. We have a generic application for the injection only. Would you please let us know that fluconazole injection is also indicated for these symptoms. If only oral suspension is indicated for the treatment of these, then we
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Chan

Answer:

As far as I can tell all three formulations are indicated for OPC and EC. I am not aware of any reasons barring applicants from applying separately for those indications using each formulation.

Imo (Ibia, Ekopino)

13. The review for the container labels and shelfpack labels was done using RLD labeling for the same packaging configuration. It appears that the RLD labeling for the glass bottle and plastic bags are not identical to each other.

14. This drug product is manufactured by Sicor Pharmaceutical, Inc. (p.1103, vol.1.2)

Date of Review: 9/27/04  Date of Submission: 8/27/04
Primary Reviewer: Chan Park  Date: 9/30/04
Team Leader: [Signature]  Date: 9/30/04

cc:
ANDA: 76-837
DUP/DIVISION FILE
HFD-813/Cpark/LGolson  (no cc)
V:\FRMSNZ\SICOR\LTRS\REV76837AP.LABELING.doc
Review

APPEARS THIS WAY
ON ORIGINAL
ANDA Number: 76-837 Date of Submission: October 19, 2004

Applicant's Name: Sicor Pharmaceuticals, Inc.

Established Name: Fluconazole Injection, 2 mg/mL (in 0.9% Sodium Chloride Injection)

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

CONTAINER LABELS - 200 mg/100 mL & 400 mg/200 mL
Satisfactory in FPL as of 8/27/04 submission (vol. 3.1)

SHELFPACK LABEL - 6 x 100 mL or 6 x 200 mL
Satisfactory in FPL as of 8/27/04 submission (vol. 3.1)

OVERWRAP POUCH
The sponsor proposed a clear pouch. Pouch is clear enough so that the text on the labels is sufficiently legible per the sponsor's statement submitted 8/27/04.

PROFESSIONAL PACKAGE INSERT LABELING
Satisfactory in FPL as of 10/19/04 submission (vol. 4.1, Rev. October, 2004)
QUESTIONS/NOTES TO THE CHEMIST - The following e-mail was to/from the chemist on the packaging material.

Question - Hi Zelleka,

Please do me a favor. The sponsor included the following language in the insert labeling regarding their container. I was informed that they do not have other approved applications which used the same packaging and the same language in the labeling. Please review the language to see this is accurate and acceptable in terms of chemistry view point. Thank you for your help, Chan

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Zelleka

FOR THE RECORD:

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3. Pertaining the description of plastic container used for this drug product, please refer to the answer from the chemist above. The sponsor's description appears accurate per the chemist.

4. This drug product is not the subject of a USP monograph.

5. The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 1054 (Volume 1.1).

6. Patent Data/Exclusivities
   None

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Imo (Ibia, Ekopino)

13. The review for the container labels and shelfpack labels was done using RLD labeling for the same packaging configuration. It appears that the RLD labeling for the glass bottle and plastic bags are not identical to each other.

14. This drug product is manufactured by Sicor Pharmaceutical, Inc. (p.1103, vol.1.2)

15. The submission of 10/19/04 is for the package insert labeling reflecting the update innovator's labeling. The sponsor submitted only pdf format electronically while submitted the side-by-side statements in MS Word in hard copy.

Date of Review: 11/10/04
Date of Submission: 10/19/04
Primary Reviewer: Chan Park
Date: 11/10/04
Team Leader: Golson Lillie
Date: 11/17/04

cc: ANDA: 76-837
DUP/DIVISION FILE
HFD-613/Cpark/LGolson (no cc)
V:\FIRMSNZ\SICOR\LTRS&REV\76837AP#2.LABELING.doc
Review

APPEARS THIS WAY ON ORIGINAL
APPLICATION NUMBER:
ANDA 76-837

CHEMISTRY REVIEWS
ANDA 76-837

Fluconazole Injection in Plastic Container
2 mg/mL

SICOR Pharmaceuticals, Inc.

Zelleka Getahun, Ph. D.
OGD - Division of Chemistry II
Table of Contents

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II. Summary of Chemistry Assessments..................................... 7
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   B. Description of How the Drug Product is Intended to be Used ... 8
   C. Basis for Approvability or Not-Approval Recommendation ... 8

III. Administrative.................................................................... 8
    A. Reviewer’s Signature ...................................................... 8
    B. Endorsement Block ...................................................... 8
    C. CC Block .................................................................. 8

Chemistry Assessment ............................................................. 9
Chemistry Review Data Sheet

1. ANDA 76-837

2. REVIEW #: 1

3. REVIEW DATE: 24-DEC-2003

4. REVIEWER: Zelleka Getahun, Ph.D.

5. PREVIOUS DOCUMENTS:
   N/A

6. SUBMISSION(S) BEING REVIEWED:

   Submission(s) Reviewed Document Date
   Original August 8, 2003

7. NAME & ADDRESS OF APPLICANT:
   Name: SICOR Pharmaceuticals, Inc.
   19 Hughes
   Address: Irvine, CA 92618 – 1902
   Representative: Rosalie A. Lowe
   Telephone: (949)-457-2808

8. DRUG PRODUCT NAME/CODE/TYPE:
   a) Proprietary Name: N/A
   b) Non-Proprietary Name (USAN): Fluconazole Injection in 0.9% Sodium Chloride
9. LEGAL BASIS FOR SUBMISSION:

Diflucan® in Sodium Chloride 0.9% in Plastic Container; NDA # 19-950 (001), Pfizer, Inc.

Patent no. 4,404,216 expires on January 29, 2004. Paragraph III certification is appended (p. 1012). The product is not covered by any exclusivity (a copy from the Orange Book is appended, p.1011).

10. PHARMACOL. CATEGORY: Antifungal

11. DOSAGE FORM: Infusion solution

12. STRENGTH/POTENCY: 2 mg/mL in 100mL and 200 mL fill infusion bags

13. ROUTE OF ADMINISTRATION: Intravenous

14. Rx/OTC DISPENSED: _x_Rx __OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____ SPOTS product – Form Completed

_x_ Not a SPOTS product

APPEARS THIS WAY ON ORIGINAL
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: Fluconazole; 2,4-Difluoro-α,α-bis(1H-1,2,4-triazol-1-ylmethyl)benzyl alcohol

Structure:

Molecular Formula: C₁₃H₁₂F₂N₆O
Molecular Weight: 306.28

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

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<th>DMF #</th>
<th>TYPE</th>
<th>HOLDER</th>
<th>ITEM REFERENCED</th>
<th>CODE¹</th>
<th>STATUS²</th>
<th>REVIEW DATE</th>
<th>COMMENTS</th>
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<tr>
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<td>Adequate*</td>
<td>29-AUG-003</td>
<td>LOA pp. 1058, 1059</td>
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<td>9705</td>
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<td>Cryovac</td>
<td>M312/plastic packaging</td>
<td>4</td>
<td>N/A</td>
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<td>LOA p. 2023</td>
</tr>
</tbody>
</table>

¹ Action codes for DMF Table:
1 – DMF Reviewed*
Other codes indicate why the DMF was not reviewed, as follows:
2 – Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

² Adequate, Inadequate or N/A
(There is enough data in the application; therefore the DMF did not need to be reviewed)

* DMF # — was reviewed by R. Rajagopalan.
B. Other Documents:

<table>
<thead>
<tr>
<th>DOCUMENT</th>
<th>APPLICATION NUMBER</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANDA</td>
<td>76-653</td>
<td>Cross referenced by SICOR on FDA 356 (h)</td>
</tr>
</tbody>
</table>

SICOR has listed ANDA 76-653 in the list of cross references on its current application. ANDA 76-653 and the current application are similar; the major difference is in the container of the drug product. In ANDA 76-653 the drug product is supplied in 100 mL and 200 mL glass vials, in the current application the drug product is supplied in plastic infusion bags.

18. STATUS:

<table>
<thead>
<tr>
<th>CONSULTS/ CMC RELATED REVIEWS</th>
<th>RECOMMENDATION</th>
<th>DATE</th>
<th>REVIEWER</th>
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<tr>
<td>Microbiology</td>
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<td>OC / J.D Ambrogio</td>
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<td>Methods Validation</td>
<td>Acceptable SOPs pp.2260 -2570</td>
<td>24-DEC-2003</td>
<td>Z. Getahun</td>
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<td>Bioequivalence</td>
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<td>Radiopharmaceutical</td>
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</tbody>
</table>

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

_x_ Yes  ____ No  If no, explain reason(s) below:
The Chemistry Review for ANDA 76-837

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is not approvable; there are pending chemistry issues.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Fluconazole is a synthetic broad spectrum antifungal agent. Fluconazole Injection (Infusion) in Sodium Chloride 0.9% in plastic containers is supplied as a 2 mg/mL solution in volumes of 100 mL and 200 mL.

The drug substance is manufactured by ____________. The drug substance is non-compendial; the manufacturer has provided the structures of the identified impurities and has also set tight specifications for total impurities. The applicant has verified that impurities in the drug substance are either non-detectable or constitute less than — % of the bulk of the drug substance.

Stability indicating method for the drug product is non-compendial. The firm has established in-house methods and methods validations. Through the forced degradation studies the drug product, is shown to be very stable; and it is also shown that the degradation profile of the drug product is identical to the RLD.

The label storage condition for the product is 5° - 25° C. The proposed expiration dating is 24 months.
B. Description of How the Drug Product is intended to be used
N/A

C. Basis for Approvability or Not-Approval Recommendation

The application is not approvable, pending satisfactory response to the chemistry issues that are raised:

__________________________________________________________

is not provided.

Labeling, Microbiology and Bioequivalence review are pending.

III. Administrative

A. Reviewer’s Signature

B. Endorsement Block

ZGetahun/1/23/04
GJSmith/1/28/04
TPalat/2/2/04

C. CC Block
Redacted 13 page(s)
of trade secret and/or
confidential commercial
information from

CHEMISTRY REVIEW #1
cc: ANDA 76-837
    ANDA DUP
    DIV FILE
    Field Copy

Endorsements (Draft and Final with Dates):

HFD-640/ZGetahun/1/23/04 ZGetahun 2/4/04
HFD-647/GJSmith/1/28/04 GJSmith 2/4/04
HFD-615/TPalat/2/2/04 TPalat 2/5/04

F/T by rad2/3/04

V:\FIRMSAM\SICOR \LTRS&REV\76837Ncr1.ZG

TYPE OF LETTER: NOT APPROVABLE - MINOR

APPEARS THIS WAY ON ORIGINAL
ANDA 76-837

Fluconazole Injection in Plastic Container
2 mg/mL

SICOR Pharmaceuticals, Inc.

Zelleka Getahun, Ph. D.
OGD - Division of Chemistry II
# Table of Contents

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   B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable .............. 7

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    B. Description of How the Drug Product is Intended to be Used .... 8
    C. Basis for Approvability or Not-Approval Recommendation ...... 8

III. Administrative ............................................................ 8
    A. Reviewer’s Signature .................................................. 8
    B. Endorsement Block ................................................... 8
    C. CC Block .............................................................. 8

Chemistry Assessment ...................................................... 9
Chemistry Review Data Sheet

1. ANDA 76-837

2. REVIEW # 2

3. REVIEW DATE: September 23, 2004

4. REVIEWER: Zelleka Getahun, Ph.D.

5. PREVIOUS DOCUMENTS:
   Original Application Document Date: August 8, 2003

6. SUBMISSION(S) BEING REVIEWED:
   Minor Amendment Document Date: August 17, 2004

7. NAME & ADDRESS OF APPLICANT:

   Name: SICOR Pharmaceuticals, Inc.
   Address: 19 Hughes
            Irvine, CA 92618 – 1902
   Representative: Rosalie A. Lowe
   Telephone: (949)-457-2808

8. DRUG PRODUCT NAME/CODE/TYPE:

   a) Proprietary Name: N/A
   b) Non-Proprietary Name (USAN): Fluconazole Injection in 0.9% Sodium Chloride

9. LEGAL BASIS FOR SUBMISSION:

   Diflucan® in Sodium Chloride 0.9% in Plastic Container; NDA # 19-950 (001), Pfizer, Inc.
   Patent no. 4404216*PED expiration date: July 29, 2004

Page 3 of 24
10. PHARMACOL. CATEGORY: Antifungal

11. DOSAGE FORM: Infusion solution

12. STRENGTH/POTENCY: 2 mg/mL in 100mL and 200 mL fill infusion bags

13. ROUTE OF ADMINISTRATION: Intravenous

14. Rx/OTC DISPENSED: x Rx  ___OTC

15. SPOTS (SPECIAL PRODUCTS ON LINE TRACKING SYSTEM)

   ___ SPOTS product – Form Completed

   x  Not a SPOTS product

APPEARS THIS WAY ON ORIGINAL
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: Fluconazole; 2,4-Difluoro-α,α-bis(1H-1,2,4-triazol-1-ylmethyl)benzyl alcohol

Structure:

Molecular Formula: C₁₃H₁₂F₂N₆O
Molecular Weight: 306.28

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

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<th>DMF #</th>
<th>TYPE</th>
<th>HOLDER</th>
<th>ITEM REFERENCED</th>
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<td></td>
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<td>12/15/04</td>
<td>LOA pp. 1058, 1059</td>
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¹ Action codes for DMF Table:
1 – DMF Reviewed
2 – Type 1 DMF
3 – Reviewed previously and no revision since last review*
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

² Adequate, Inadequate or N/A
(There is enough data in the application; therefore the DMF did not need to be reviewed)

* DMF # ___ was reviewed by R. Rajagopalan.
Annual report submitted by the DMF holder on 5-MAR-2004, not reviewed.
B. Other Documents:

<table>
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<th>DESCRIPTION</th>
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<tbody>
<tr>
<td>ANDA</td>
<td>76-653</td>
<td>Cross referenced by SICOR on FDA 356 (h)</td>
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</table>

SICOR has listed ANDA 76-653 in the list of cross references on its current application. ANDA 76-653 and the current application are similar; the major difference is in the container of the drug product. In ANDA 76-653 the drug product is supplied in 100 mL and 200 mL glass vials, in the current application the drug product is supplied in plastic infusion bags.

18. STATUS:

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19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.  
\[ \text{x Yes} \quad \text{No} \]  If no, explain reason(s) below:
The Chemistry Review for ANDA 76-837

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Approvable. There are no pending chemistry issues.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Fluconazole is a synthetic broad spectrum antifungal agent. Fluconazole Injection (Infusion) in Sodium Chloride 0.9% in plastic containers is supplied as a 2 mg/mL solution in volumes of 100 mL and 200 mL.

The drug substance is manufactured by ____________. The drug substance is non-compendial; the manufacturer has provided the structures of the identified impurities and has also set tight specifications for total impurities. The applicant has verified that the impurities in the drug substance are either non-detectable or constitute less than —% of the bulk of the drug substance.

[Blank]

The firm has established in-house analytical methods that are stability indicating. Satisfactory methods validation data are included. The forced degradation studies of the drug product show that it is very stable. Forced degradations of the DP and the RLD show that the degradation profile of the DP is identical to that of the RLD. The label storage condition for the product is 5° - 25° C. The proposed expiration dating is 24 months.

B. Description of How the Drug Product is intended to be used

N/A
C. Basis for Approvability or Not-Approval Recommendation

The application is **approvable**. Sicor has submitted fairly satisfactory responses to all the comments made by Review #1. The specifications limits for total impurities (expiration dating is 24 months). The analytical methods used are satisfactory.

III. Administrative

A. Reviewer's Signature

[Signature]
12/23/04

B. Endorsement Block

ZGetahun/9/28/04
GJSmith/12/15/04
TPalat/12/20/04

C. CC Block

APPEARS THIS WAY
ON ORIGINAL
Redacted 13 page(s) of trade secret and/or confidential commercial information from

CHEMISTRY REVIEW #2
33. ESTABLISHMENT INSPECTION  
Acceptable

34. BIOEQUIVALENCE

Acceptable 18-Jun-04

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

The firm seeks categorical exclusion under 21 CFR § 25.31 (a). The RLD for the same indications, level of dosage and duration of administration is on the market; and the data available establish that at the level of exposure the substance does not pose a toxicity risk to organisms in the environment. The firm also states that it is in compliance with all applicable Federal, State and local environmental rules and regulations (p. 2637).
cc:    ANDA 76-837
      ANDA DUP
      DIV FILE
      Field Copy

Endorsements (Draft and Final with Dates):

HFD-640/ZGetahun/  12/23/04
HFD-647/GJSmith/  12/27/04
HFD-615/TPalat/  12/27/04

F/T by

V:\FIRMSAM\SICOR\LTRS&REV\76837Ncr2.ZG

TYPE OF LETTER: APPROVABLE

APPEARS THIS WAY
ON ORIGINAL

23 of 23
APPLICATION NUMBER:
ANDA 76-837

BIOEQUIVALENCE REVIEW
OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #: 76-837
SPONSOR: SICOR Pharmaceuticals, Inc.

DRUG AND DOSAGE FORM: Fluconazole Injection in Sodium Chloride 0.9% in plastic containers

STRENGTH(S): 2 mg/mL, 100 mL and 200 mL

STUDY SUMMARY: The test drug product is a parental solution intended solely for administration by injection and contains the same active an inactive ingredients in the same concentration as the approved reference listed product. A waiver of the in-vivo bioavailability/bioequivalence study requirements is granted [21 CFR 320.22(b)(1)]

DSI INSPECTION STATUS

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<td>For cause ___</td>
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<td>Other ___</td>
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</table>

PROJECT MANAGER: Aaron Sigler, Pharm.D.
BRANCH: I

INITIAL: 8  DATE: 6/17/04

SPECIAL ASSISTANT TO THE DIRECTOR: Lizzie Sanchez, Pharm.D.

INITIAL: 6/17/04

DIRECTOR, DIVISION OF BIOEQUIVALENCE: DALE P. CONNER, Pharm.D.

INITIAL: 6/17/04
BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 76-837

APPLICANT: SICOR Pharmaceuticals, Inc.

DRUG PRODUCT: Fluconazole for Injection in Sodium Chloride in plastic containers, 2 mg/mL, 100 mL and 200 mL

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

[Signature]

Dale P. Conner, Pharm. D.
Director,
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 76-837

MICROBIOLOGY REVIEW
Product Quality Microbiology Review
Review for HFD-640

October 8, 2004

ANDA: 76-837

Drug Product Name
Proprietary: N/A
Non-proprietary: Fluconazole Injection 2 mg/mL
Drug Product Classification: N/A

Review Number: #1

Subject of this Review
Submission Date: August 29, 2003
Receipt Date: September 2, 2003
Consult Date: N/A
Date Assigned for Review: June 25, 2004

Submission History (for amendments only)
Date(s) of Previous Submission(s): N/A
Date(s) of Previous Micro Review(s): N/A

Applicant/Sponsor
Name: SICOR Pharmaceuticals, Inc.
Address: 19 Hughes, Irvine CA 92618-1902
Representative: Rosalie Lowe, Director, Regulatory Affairs
Telephone: 949-457-2808

Name of Reviewer: Lisa S.G. Shelton

Conclusion: The submission is recommended for approval on the basis of sterility assurance.
Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: N/A

2. SUPPLEMENT PROVIDES FOR: N/A

3. MANUFACTURING SITE:
   SICOR Pharmaceuticals, Inc.
   19 Hughes
   Irvine, CA 92618-1902

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND
   STRENGTH/POTENCY: Sterile liquid, intravenous, 2 mg/mL
   packaged as 200 mg/100 mL in a 100 mL infusion bag and 400 mg/200
   mL in a 250 mL infusion bag, single dose containers

5. METHOD(S) OF STERILIZATION: ————

6. PHARMACOLOGICAL CATEGORY: Antifungal

B. SUPPORTING/RELATED DOCUMENTS:
   DMF ————
   DMF 9705 – Cryovac
   DMF ————
   ANDA 76-653 – Fluconazole Injection 2 mg/mL in 100 mL and 200 mL vials.

C. REMARKS:
   Parts of this review are similar to that of N.Nath (Microbiology Review
   #1, 8/28/03) for ANDA 76-653 Fluconazole Injection 2 mg/mL in 100 and 200
   mL vials.
   The applicant was contacted by telephone to clarify if the units used for
   the ———— validation were overwrapped and ———— (10/7/04). Their response is incorporated into the subject review.

filename: V:\MICROREV\76-837.doc
Executive Summary

I. Recommendations

A. Recommendation on Approvability –
   The submission is **recommended** for approval on the basis of sterility assurance. Specific comments are provided in the "Product Quality Microbiology Assessment" section.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –

B. Brief Description of Microbiology Deficiencies – N/A

C. Assessment of Risk Due to Microbiology Deficiencies –
   The safety risk on the basis of sterility assurance is considered minimal.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block
   Microbiologist, Lisa S.G. Shelton, Ph.D. 10/2/04
   Microbiology Team Leader, Neal J. Sweeney, Ph.D.

C. CC Block
   cc: Original ANDA 76-837
   Division File
   Field Copy
Redacted 13 page(s)
of trade secret and/or
confidential commercial
information from

MICROBIOLOGY REVIEW #1
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 76-837

ADMINISTRATIVE DOCUMENTS
OGD APPROVAL ROUTING SUMMARY

ANDA # 76-837  Applicant: SICOR Pharmaceuticals Inc.
Drug: Fluorouracil Injection  Strength(s): 2 mg/ml

APPROVAL □  TENTATIVE APPROVAL □  SUPPLEMENTAL APPROVAL (NEW STRENGTH) □  OTHER □

REVIEWER:

1. Martin Shimer
   Chief, Reg. Support Branch
   Contains GDEA certification: Yes □ No □
   Determined of Involvement? Yes □ No □
   Pediatric Exclusivity System: RLD = 19-950
   Patent/Exclusivity Certification: Yes □ No □
   If Para. IV Certification did applicant Nothing Submitted
   Notify patent holder/NDA Holder: Yes □ No □
   Written request issued: □
   Was applicant sued w/in 45 days: Yes □ No □
   Study Submitted: □
   Has case been settled: Yes □ No □ Date settled: 180 day
   Generic Drugs Exclusivity for each strength: Yes □ No □
   Date of latest Labeling Review/Approval Summary: 11/27/2004
   Any filing status changes requiring addition Labeling Review: Yes □ No □
   Type of Letter: □
   Comments:

   Date: 12/20/04
   Initials: GP

2. Project Manager, Tel Staff Team
   Review Support Branch
   Original Rec'd date: 2-29-04
   Date Acceptable for Filing: 9-2-03
   Patent Certification (type): □
   Date Patent/Exclusivity expires: □
   Citizens' Petition/Legal Case: Yes □ No □
   (If YES, attach email from PM to CP coord)
   First Generic: Yes □ No □
   Labeling Acceptable Email Rec'd Yes □ No □
   Labeling Acceptable Email filed Yes □ No □
   Date of Sterility Assur. App.: 11/14/04
   Methods Val. Samples Pending: Yes □ No □
   MV Commitment Rcd. from Firm: Yes □ No □
   Acceptable Bio reviews tabbed: Yes □ No □
   Modified-release dosage form: Yes □ No □
   Suitability Petition/Pediatric Waiver: Interim Dissol. Specs in AP Ltr: Yes □
   Pediatric Waiver Request Accepted □ Rejected □ Pending □
   Previously reviewed and tentatively approved: □
   Date: □
   Previously reviewed and CGMP def. /NA Minor issued: □
   Date: □
   Comments:

   Date: □
   Initials: □

3. David Read (PP IVs Only) Pre-MMA Language included □
   OGD Regulatory Counsel, Post-MMA Language Included □
   Comments:

   NA

4. Div. Dir/Deputy Dir
   Chemistry DIV. I II or III
   Comments:

   Date: 1/1/06
   Initials: RKA
5. Frank Holcombe  First Generics Only
Assoc. Dir. For Chemistry
Comments: (first generic drug review)
N/A. Multiple ANDAs have been approved for this drug product.

6. Vacant
Deputy MR, DLPS
R&D Central Research
Sodium Chloride 0.9% 200ml Comp. 19-958-012-01

7. Peter Rickman
Director, DLPS
Para IV Patent Cert: Yes □ No □ Pending Legal Action: Yes □ No □ Petition: Yes □ No □
Comments: FE found acceptable for approval 1/17/03 as endorsed 1/29/04. Bioequivalence
 was granted number 21 CFI 2320 22 (NC). SCL and BBI endorsed.

8. Robert L. West
Deputy Director, OGD
Para IV Patent Cert: Yes □ No □ Pending Legal Action: Yes □ No □ Petition: Yes □ No □
Comments: Acceptable EES dated 1/13/05 (Notified 1/13/05). No O.P.I.

9. Gary Buehler
Director, OGD
Comments:
First Generic Approval □ PD or Clinical for BE □ Special Scientific or Reg. Issue □

10. Project Manager, Team
Review Support Branch
Date PETS checked for first generic drug (just prior to notification to firm)
Applicant notification:
□ Time notified of approval by phone YES □ Time approval letter faxed
FDA Notification:
□ Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
□ Date Approval letter copied to \CDS014\DRUGAPP\ directory.
August 29, 2003

Mr. Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
Attention: Documentation and Control Room 150
7500 Standish Place
Rockville, MD 20855-2773

RE: Fluconazole Injection
2 mg/mL
ANDA: Number to be Assigned.

Dear Mr. Buehler:

In accordance with Section 314.92 of the Code of Federal Regulations, Title 21, we hereby submit an Abbreviated New Drug Application for Fluconazole Injection, 2 mg/mL, a parenteral preparation supplied as:

<table>
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<th>Strength</th>
<th>Total Drug Content</th>
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<td>2 mg/mL</td>
<td>200 mg per infusion bag</td>
<td>100 mL infusion bag packaged 6 per shelf pack</td>
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<tr>
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<td>400 mg per infusion bag</td>
<td>250 mL infusion bag packaged 6 per shelf pack</td>
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</table>

On July 2, 2003, we notified the Agency that Gensia Sicor Pharmaceuticals, Inc. changed the corporate company name to SICOR Pharmaceuticals, Inc. Please note that this submission reflects the new corporate company name, SICOR Pharmaceuticals, Inc. Although we have initiated changes to documents revising the corporate company name to SICOR Pharmaceuticals, Inc, there are still some documents in this submission with the previous company name, Gensia Sicor Pharmaceuticals, Inc.

SICOR’s proposed drug product is the generic version of Pfizer’s Diflucan® in Sodium Chloride 0.9% in Plastic Container, pursuant to NDA No. 19-950 (002). Pfizer’s drug product appears in the FDA listing titled Approved Drug Products with Therapeutic Equivalence Evaluation, 23rd Edition. The approved drug product marketed by Pfizer is available in a 100 mL and 200 mL Viaflex® Plus plastic container.

Our proposed drug product, Fluconazole Injection, has the same active and inactive ingredients, dosage form, strength, route of administration, and conditions of use as Pfizer’s listed drug product.
Fluconazole Injection will be packaged in a 100 mL and 250-mL flexible, polymer bag with a single port fitting (combination filling port and twist-off connector spike port. The infusion bags are composed of sterilizable medical grade film (Cryovac® M312 Pharmaceutical Solutions Film). Cryovac Sealed Air Corporation manufactures this film. The information for the M312 film is provided in Drug Master File (DMF) No. 9705. The spike port is manufactured by . The connector tubing is manufactured by (DMF No.).

Two (2) stability lots of Fluconazole Injection were manufactured and data are presented in Section XVII of this application.

Four (4) copies of the proposed labeling have also been provided in Section V of the application in both the archival and review copies.

The application consists of three (3) volumes and has been formatted in accordance with the Office of Generic Drug's Guidance for Industry, Organization of an ANDA, OGD #1, issued February 1999. Copies are provided as follows:

1) One (1) Archival Copy bound in Blue Jackets
2) One (1) Review Copy bound in Red Jackets

A true copy of this application, which was bound in Burgundy Jackets, has been submitted to the U.S. Food and Drug Administration of Irvine, California, District Office.

Since the stability indicating method for the product is non-compendial, three (3) additional methods validation packages have been included and are marked "Analytical Methods". These three additional copies are identical to Section XVI as presented in the archival and review copies, and have been separately bound in Black Jackets.

We trust you will find the information in this application satisfactory for your review and approval. If there are any questions concerning this application, please do not hesitate in contacting me at (949) 457-2808. I can also be contacted by facsimile at (949) 583-7351.

Sincerely,

Rosalie A. Lowe
Director, Regulatory Affairs

cc: Mr. Alonza Cruse
District Director
U.S. Food and Drug Administration, Los Angeles District
19900 MacArthur Blvd., Suite 300
Irvine, CA 92615
December 8, 2003

Mr. Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
Attention: Documentation and Control Room 150
7500 Standish Place
Rockville, MD 20855-2773

RE: Fluconazole Injection
2 mg/mL
ANDA: 76-837

AMENDMENT-Chemistry

Dear Mr. Buehler:

Reference is made to our abbreviated new drug application, ANDA 76-837, for Fluconazole Injection, 2 mg/mL, submitted on August 29, 2003.

We hereby amend this application, in accordance with the provisions of Section 314.96(a)(1) of the Code of Federal Regulations, Title 21. Specifically, we wish to include an alternate
We trust you will find the information in this amendment satisfactory for your review and approval. If there are any questions concerning this amendment, please do not hesitate in contacting me at (949) 455-4724. We can also be contacted by facsimile at (949) 583-7351.

Sincerely,

Elvia O. Gustavson
Director, Regulatory Affairs

cc: Mr. Alonza Cruse
District Director
FDA, Los Angeles District
19900 MacArthur Blvd., Suite 300
Irvine, CA 92612
July 14, 2004

Mr. Gary Buehler, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
Attention: Documentation and Control Room 150
7500 Standish Place
Rockville, MD 20855-2773

RE: Fluconazole for Injection in Plastic Container
ANDA: 76-837

MINOR AMENDMENT

Dear Mr. Buehler:

Reference is made to our abbreviated new drug application, ANDA 76-837, for Fluconazole for Injection in Plastic Container, 2 mg/mL, submitted on August 29, 2003. Reference is also made to the deficiency letter dated March 3, 2004.

In accordance with the provisions of Section 314.96(a)(1) of the Code of Federal Regulations, Title 21, we hereby amend this application to provide the labeling information. Twelve (12) samples of the final printed labels and labeling are provided in Attachment 1 for your review. Additionally, a side-by-side labeling comparison of our proposed labeling with our previous submission is provided for your review in Attachment 2, with all differences annotated and explained.

We trust you will find the information in this amendment satisfactory for your review and approval. If there are any questions concerning this amendment, please do not hesitate in contacting me at (949) 457-2808. We can also be contacted by facsimile at (949) 583-7351.

Sincerely,

Rosalie A. Lowe
Director, Regulatory Affairs

cc: Mr. Alonza Cruse
District Director
FDA, Los Angeles District
19900 MacArthur Blvd., Suite 300, Irvine, CA 92612

RECEIVED
JUL 15 2004
OGD/CDER
August 17, 2004

Mr. Gary Buehler, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
Attention: Documentation and Control Room 150
7500 Standish Place
Rockville, MD 20855-2773

RE: Fluconazole for Injection in Plastic Container
ANDA: 76-837

MINOR AMENDMENT

Dear Mr. Buehler:

Reference is made to our abbreviated new drug application, ANDA 76-837, for Fluconazole for Injection in Plastic Container, 2 mg/mL, submitted on August 29, 2003. Reference is also made to the deficiency letter dated February 5, 2004.

In accordance with the provisions of Section 314.96(a)(1) of the Code of Federal Regulations, Title 21, we hereby amend this application to provide the chemistry information.

We trust you will find the information in this amendment satisfactory for your review and approval. If there are any questions concerning this amendment, please do not hesitate in contacting me at (949) 457-2808. We can also be contacted by facsimile at (949) 583-7351.

Sincerely,

Rosalie A. Lowe
Director, Regulatory Affairs

cc: Mr. Alonza Cruse
District Director
FDA, Los Angeles District
19900 MacArthur Blvd., Suite 300, Irvine, CA 92612
August 27, 2004

Mr. Gary Buehler, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
Attention: Documentation and Control Room 150
7500 Standish Place
Rockville, MD 20855-2773

RE: Fluconazole for Injection in Plastic Container
ANDA: 76-837

MINOR AMENDMENT

Dear Mr. Buehler:

Reference is made to our abbreviated new drug application, ANDA 76-837, for Fluconazole for Injection in Plastic Container, 2 mg/mL, submitted on August 29, 2003. Reference is also made to the deficiency letter dated July 14, 2004.

In accordance with the provisions of Section 314.96(a)(1) of the Code of Federal Regulations, Title 21, we hereby amend this application to provide the labeling information. Twelve (12) samples of the final printed labels and labeling are provided in Attachment 1 for your review. Additionally, a side-by-side labeling comparison of our proposed labeling with our previous submission is provided for your review in Attachment 2, with all differences annotated and explained.

We trust you will find the information in this amendment satisfactory for your review and approval. If there are any questions concerning this amendment, please do not hesitate in contacting me at (949) 457-2808 or Mirabelle Pao, Project Specialist at (949) 457-2848. We can also be contacted by facsimile at (949) 583-7351.

Sincerely,

Rosalie A. Lowe
Director, Regulatory Affairs

Rosalie A. Lowe
Director, Regulatory Affairs

S:/Fluconazole Bags/Amends/Amend5.doc

cc: Mr. Alonza Cruse
District Director
FDA, Los Angeles District
19900 MacArthur Blvd., Suite 300, Irvine, CA 92612

RECEIVED
AUG 30 2004
OGD/CDER
October 19, 2004

Mr. Gary Buehler, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
Attention: Documentation and Control Room 150
7500 Standish Place
Rockville, MD 20855-2773

RE: Fluconazole for Injection in Plastic Container
ANDA: 76-837

MINOR AMENDMENT

Dear Mr. Buehler:

Reference is made to our abbreviated new drug application, ANDA 76-837, for Fluconazole for Injection in Plastic Container, 2 mg/mL, submitted on August 29, 2003. Reference is also made to the minor amendment submitted on August 27, 2004.

In accordance with the provisions of Section 314.96(a)(1) of the Code of Federal Regulations, Title 21, we hereby amend this application to provide our most current labeling information. The package insert labeling was revised to incorporate the Safety-Related Change from the RLD labeling, Diflucan®, approved on October 7, 2004.

A CD copy of the final printed labeling is provided for your review. Additionally, a side-by-side labeling comparison of our proposed labeling with our previous submission is provided for your review in Attachment 1, with all differences annotated and explained.

We trust you will find the information in this amendment satisfactory for your review and approval. If there are any questions concerning this amendment, please do not hesitate in contacting me at (949) 457-2808 or Mirabelle Pao, Project Specialist at (949) 457-2848. We can also be contacted by facsimile at (949) 583-7351.

Sincerely,

Rosalie A. Lowe
Director, Regulatory Affairs

CC: Mr. Alonza Cruse
District Director
FDA, Los Angeles District
19900 MacArthur Blvd., Suite 300, Irvine, CA 92612
December 3, 2004

Mr. Gary Buehler, Director  
Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Metro Park North II, HFD-600  
Attention: Documentation and Control Room 150  
7500 Standish Place  
Rockville, MD 20855-2773

RE:  Fluconazole for Injection in Plastic Container  
ANDA: 76-837

PATENT AMENDMENT

Dear Mr. Buehler:

Reference is made to our abbreviated new drug application, ANDA 76-837, for Fluconazole for Injection in Plastic Container, 2 mg/mL, submitted on August 29, 2003.

In accordance with the provisions of Section 314.94 (a)(12)(viii)(C) of the Code of Federal Regulations, Title 21, we hereby amend this application to provide a revised patent certification due to the expiration of U.S. Patent No. 4,404,216. Enclosed is the requisite Paragraph II Certification.

We trust you will find the information in this amendment satisfactory for your review and approval. If there are any questions concerning this amendment, please do not hesitate in contacting me at (949) 457-2808 or Tania Hoffman, Manager at (949) 455-4728. We can also be contacted by facsimile at (949) 583-7351.

Sincerely,

[Signature]

Roseli A. Lowe  
Director, Regulatory Affairs

S:\Fluconazole Bags 76-837\Amends\Amend7.doc  
cc: Mr. Alonza Cruse  
District Director  
FDA, Los Angeles District  
19900 MacArthur Blvd., Suite 300, Irvine, CA 92612

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DEC 06 2004  
OGD / CDER