**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-735/S-055

Ortho McNeil Pharmaceutical, Inc.
c/o Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
Attention: Ms. Cynthia Chianese
Director, Regulatory Affairs
1000 U.S. Highway 202 South, P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Chianese:

Please refer to your supplemental drug application, dated January 5, 2006 and received January 6, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

| NDA Number | Supplement Number | Drug Product |
|---|---|---|
| 19-735 | 055 | Floxin® (ofloxacin) Tablets, 200 mg, 300 mg, and 400 mg |

We acknowledge receipt of your submission dated June 8, 2006.

This supplemental application provides for the following revisions to the text for the package insert (~~strikethrough~~ = deleted and double-underlined = added):

1. The **CLINICAL PHARMACOLOGY/MICROBIOLOGY/Susceptibility Tests/Dilution Techniques** subsection of the package insert was revised as follows:

   Dilution Techniques:

   Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MIC values). These MIC values provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MIC values should be determined using a standardized procedure. Standardized procedures are based on a dilution method[1] (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of ofloxacin powder. The MIC values should be interpreted according to the following criteria:

~~For testing aerobic microorganisms other than *Haemophilus influenzae*, *Neisseria gonorrhoeae*, and *Streptococcus pneumoniae*:~~ For testing *Enterobacteriaceae*, methicillin-susceptible *Staphylococcus aureus*, and *Pseudomonas aeruginosa*:

| MIC (µg/mL) | Interpretation |
|---|---|
| ≤ 2 | Susceptible (S) |
| 4 | Intermediate (I) |
| ≥ 8 | Resistant (R) |

For testing *Haemophilus influenzae*:[a]

| MIC (µg/mL) | Interpretation |
|---|---|
| ≤ 2 | Susceptible (S) |

[a] This interpretive standard is applicable only to broth microdilution susceptibility tests with *Haemophilus influenzae* using *Haemophilus* Test Medium[1]

The current absence of data on resistant strains precludes defining any results other than "Susceptible". Strains yielding MIC results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

For testing *Neisseria gonorrhoeae*:[b]

| MIC (µg/mL) | Interpretation |
|---|---|
| ≤ 0.25 | Susceptible (S) |
| 0.5-1 | Intermediate (I) |
| ≥ 2 | Resistant (R) |

[b] These interpretive standards are applicable only to agar dilution tests using GC agar base and 1% defined growth supplement incubated in 5% $CO_2$.

For testing *Streptococcus* ~~species including *Streptococcus* *pneumoniae*~~ and *Streptococcus pyogenes*:[c]

| MIC (µg/mL) | Interpretation |
|---|---|
| ≤ 2 | Susceptible (S) |
| 4 | Intermediate (I) |
| ≥ 8 | Resistant (R) |

[c] These interpretive standards are applicable only to broth microdilution susceptibility tests using cation-adjusted Mueller-Hinton broth with 2-5% lysed horse blood.

2. The **CLINICAL PHARMACOLOGY/MICROBIOLOGY/Susceptibility Tests/Diffusion Techniques** subsection of the package insert was revised as follows:

Diffusion Techniques:

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure[2] requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 5-µg ofloxacin to test the susceptibility of microorganisms to ofloxacin.

Reports from the laboratory providing results of the standard single-disk susceptibility test with a 5-µg ofloxacin disk should be interpreted according to the following criteria:

~~For testing aerobic microorganisms other than *Haemophilus influenzae*, *Neisseria gonorrhoeae*, and *Streptococcus pneumoniae*:~~ For testing *Enterobacteriaceae*, methicillin-susceptible *Staphylococcus aureus*, and *Pseudomonas aeruginosa:*

| Zone Diameter (mm) | Interpretation |
|---|---|
| ≥16 | Susceptible (S) |
| 13-~~16~~15 | Intermediate (I) |
| ≤12 | Resistant (R) |

For testing *Haemophilus influenzae*:[g]

| Zone Diameter (mm) | Interpretation |
|---|---|
| ≥ 16 | Susceptible (S) |

[g] This zone diameter standard is applicable only to disk diffusion tests with *Haemophilus influenzae* using *Haemophilus* Test Medium (HTM)[2] incubated in 5% $CO_2$.

The current absence of data on resistant strains precludes defining any results other than "Susceptible". Strains yielding zone diameter results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

For testing *Neisseria gonorrhoeae*:[h]

| Zone Diameter (mm) | Interpretation |
|---|---|
| ≥ 31 | Susceptible (S) |
| 25-30 | Intermediate (I) |
| ≤ 24 | Resistant (R) |

[h] These zone diameter standards are applicable only to disk diffusion tests using GC agar base and 1% defined growth supplement incubated in 5% $CO_2$

For testing *Streptococcus* ~~species~~ *pneumoniae* ~~including~~ and *Streptococcus pyogenes*:[i]

| Zone Diameter (mm) | Interpretation |
|---|---|
| ≥ 16 | Susceptible (S) |
| 13-15 | Intermediate (I) |
| ≤ 12 | Resistant (R) |

[i] These zone diameter standards are applicable only to disk diffusion tests performed using Mueller-Hinton agar supplemented with 5% defibrinated sheep blood and incubated in 5% $CO_2$.

3. The **INDICATIONS AND USAGE** section of the package insert was revised as follows:

   **Uncomplicated skin and skin structure infections** due to methicillin-susceptible *Staphylococcus aureus, Streptococcus pyogenes,* or *Proteus mirabilis.*

We have completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text. The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: ***Providing Regulatory Submissions in Electronic Format - NDAs*** (January 1999) and ***Providing Regulatory Submissions in Electronic Format – Content of Labeling*** (February 2004). The guidances specify that labeling be submitted in *pdf* format. To assist in our review of the FPL and future submissions, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper. For administrative purposes, this submission should be designated "**FPL for approved supplement NDA 19-735/S-055**." Approval of this submission by the FDA is not required before the labeling is used.

The electronic labeling rule published December 11, 2003 (FR 69009) requires submission of content of labeling [21 CFR 201.100(d)(3)] in electronic format effective June 8, 2004. For additional information, consult the guidance for industry *Providing Regulatory Submissions in Electronic Format - Content of Labeling* (April 2005). The guidance specifies that, as of fall 2005, content of labeling is to be submitted in structured product labeling (SPL) format. To facilitate our review of your submission, we ask that labeling also be submitted in MS Word format with proposed revisions clearly indicated.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Rebecca D. Saville, Pharm.D., Regulatory Project Manager, at (301) 796-1600.

Sincerely,

*{See appended electronic signature page}*

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure

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

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/s/

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Renata Albrecht

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