

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
21-061 and 21-062

CORRESPONDENCE

Bristol-Myers Squibb
Pharmaceutical Research Institute

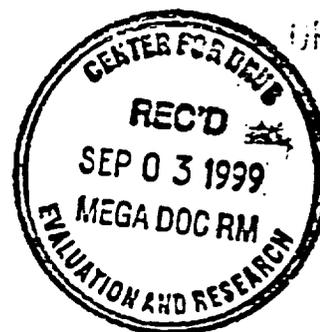
P.O. Box 5400 Princeton, NJ 08540 609 818 3000

TEQUIN™ (gatifloxacin) Tablets and I.V.
NDA #21-061/21-062

Amendment No. 37

September 2, 1999

Mark J. Goldberger, M.D., Director
Division of Special Pathogens and
Immunologic Drug Products
HFD-590
Center for Drug Evaluation and Research
Attention: Document Control Room
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20850



Dear Dr. Goldberger:

Reference is made to NDA No. 21-061, TEQUIN™ (gatifloxacin) Tablets and to NDA No. 21-062, TEQUIN™ (gatifloxacin) I.V., and to a facsimile from Ms. Brenda Atkins (August 26, 1999) containing requests from Dr. John Smith, the Chemistry Reviewer and Dr. Norman Schmuft, the Chemistry Team Leader to withdraw the Environmental Assessment (EA) and substitute a claim of categorical exclusion.

Bristol-Myers Squibb Company, via this amendment, requests to withdraw the Environmental Assessment (EA) for NDAs No. 21-061 and No. 21-062. This request is based upon our review of latest forecasts for use and distribution of TEQUIN™ (gatifloxacin) in the United States. A claim for categorical exclusion is included on the next page.

If you have any questions regarding this submission, please contact me at (609) 818-3799.

Sincerely,

Satyam M. Upadrashta, Ph.D.
Associate Director, CMC
Worldwide Regulatory Affairs

DUPLICATE



Bristol-Myers Squibb Pharmaceutical Research Institute

0000003

Richard L. Gelb Center for Pharmaceutical Research and Development

5 Research Parkway P.O. Box 5100 Wallingford, CT 06492-7660

TEQUIN (gatifloxacin) Tablets
NDA # 21-061

Amendment # 038
- Response to Request for Information

September 3, 1999

Mark J. Goldberger, M.D., Director
Division of Special Pathogens and Immunologic Drug Products, HFD-590
Center for Drug Evaluation and Research
Attention: Document Control Room
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20850

Dear Dr. Goldberger:

Reference is made to NDA # 21-061, TEQUIN™ (gatifloxacin) Tablets and to NDA # 21-062, TEQUIN™ (gatifloxacin) Injection. Reference is also made to an August 13, 1999 FDA facsimile containing requests from Dr. Joyce Korvick for additional analyses of liver function data and for analyses of laboratory data that may pertain to the temafloxacin syndrome/hemolytic uremic syndrome.

This submission contains the following:

Attachment A: A copy of the August 13th FDA facsimile

Attachment B: Bristol-Myers Squibb responses to the information requested in this facsimile. Please be advised that a diskette is being provided directly to Dr. Korvick that contains the tables requested in the facsimile.

If you have any questions, please contact me at (203) 677-6883.

Sincerely,



Douglas G. Kriesel, Ph.D.
Director
Worldwide Regulatory Affairs

cc: Dr. Joyce Korvick (entire submission including diskette)
Ms. Brenda Atkins (cover letter)

8 pages have been removed here because they contain confidential information that will not be included in the redacted portion of the document for the public to obtain.



Hospital Products Division

Abbott Laboratories
Dept. 39E, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

December 6, 1999

Mr. John Smith/Ms. Laurie Bernato
Center for Drug Evaluation and Research
Division of Special Pathogen and Immunologic Drug Products
Attention: Document Control Room
5600 Fishers Lane, HFD-590
Rockville, Maryland 20857

Phone: 301-827-2387
Fax: 301-827-2475

*Sent via Federal Express
and Facsimile*

RE: TYPE II DRUG MASTER FILE [redacted]
Chemistry, Manufacturing and Controls for:
TEQUIN™ I.V. (gatifloxacin)

Dear Mr. Smith/Ms. Bernato:

Reference is made to our original Type II Drug Master File [redacted] (dated December 21, 1999) for Tequin I.V. (gatifloxacin), manufactured in North Chicago, IL, in support of Bristol-Myers Squibb Company's drug product applications. Reference is also made to the FDA correspondence dated November 18, 1999, regarding our above referenced DMF.

This letter is to inform you that Abbott Laboratories has amended the above referenced DMF on December 6, 1999, per the FDA correspondence dated November 18, 1999. Per the referenced FDA correspondence, this DMF amendment has been sent to the FDA, Center for Drug Evaluation and Research, Central Document Room, Drug Master File Staff.

Please contact me if I can be of further assistance.

Sincerely,

ABBOTT LABORATORIES

Christopher L. Markos
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 938-2759
Fax: (847) 938-7867
E-Mail: markoc@hpd.abbott.com

Bristol-Myers Squibb Pharmaceutical Research Institute

Richard L. Gelb Center for Pharmaceutical Research and Development
5 Research Parkway P.O. Box 5100 Wallingford, CT 06492-7660

TEQUIN™ (gatifloxacin) Tablets
NDA No. 21-061

Amendment No. 67 -
WITHDRAWAL OF
PENICILLIN-RESISTANT
STRAINS INDICATION

December 16, 1999

Mark J. Goldberger, M.D., Director
Division of Special Pathogens and
Immunologic Drug Products
HFD-590
Center for Drug Evaluation and Research
Attention: Document Control Room
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20850

Bristol-Myers Squibb
Pharmaceutical Research Institute
Richard L. Gelb Center for Pharmaceutical Research and Development

Dear Dr. Goldberger:

Reference is made to TEQUIN™ (gatifloxacin) Tablets, NDA # 21-061, and TEQUIN™ (gatifloxacin) Injection, NDA # 21-062. Reference is also made to a December 15, 1999 FDA facsimile on Phase 4 commitments and to the December 16, 1999 teleconference with representatives from the Division of Special Pathogens and Immunologic Drug Products.

Please be advised that effective of the date of this communication, Bristol-Myers Squibb hereby withdraws the request for approval of penicillin-resistant strains of *Streptococcus pneumoniae* which appeared in the community-acquired pneumonia, acute bacterial exacerbation of chronic bronchitis, and acute sinusitis indications in the TEQUIN proposed package insert that was provided in the original NDA submissions on December 28, 1998.

If you have any questions concerning this submission, please contact me at (203) 677-6883.

Sincerely,



Douglas C. Kriesel, Ph.D.
Director, Regulatory Science

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A Bristol-Myers Squibb Company

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Bristol-Myers Squibb Pharmaceutical Research Institute

Richard L. Gelb Center for Pharmaceutical Research and Development

5 Research Parkway P.O. Box 5100 Wallingford, CT 06492-7660

**TEQUIN™ (gatifloxacin) Tablets
NDA No. 21-061**

**Amendment No. 66 -
Phase 4 Commitment**

December 16, 1999

Mark J. Goldberger, M.D., Director
Division of Special Pathogens and
Immunologic Drug Products
HFD-590
Center for Drug Evaluation and Research
Attention: Document Control Room
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20850

BEST POSSIBLE COPY

Bristol-Myers Squibb

Dear Dr. Goldberger:

Pharmaceutical Research Institute

Reference is made to TEQUIN™ (gatifloxacin) Tablets, NDA # 21-061, and TEQUIN™ (gatifloxacin) Injection, NDA # 21-062. Reference is also made to a December 15, 1999 FDA facsimile on Phase 4 commitments and to the December 16, 1999 teleconference with representatives from the Division of Special Pathogens and Immunologic Drug Products.

Please be advised that Bristol-Myers Squibb agrees to the following Phase 4 commitments:

1. To better understand this risk/benefit profile of oral gatifloxacin, post-marketing adverse event data should be available following at least 1 million patients exposures worldwide. A substantial proportion of these exposures should be from the United States. The results of this study should be submitted to the Division by December 31, 2000.
2. Bristol-Myers Squibb will conduct and submit the results of an active surveillance program. The results of this program will provide information on incidence of adverse events using gatifloxacin tablets and/or gatifloxacin injectable for at least 15,000 gatifloxacin exposures. Please submit protocols and methods for this ongoing study to the Division within ninety days of receipt of this letter. A report on this experience will be submitted to the Division by December 31, 2000.
3. Bristol-Myers Squibb will conduct a study of the effect of gatifloxacin on the QT interval, by studying its effect in patients receiving gatifloxacin in currently ongoing studies. Paired, valid electrocardiograms should be performed along with serum concentrations at the time of the electrocardiogram. The results of this study should be submitted to the Division by December 31, 2000.
4. Bristol-Myers Squibb will conduct a gatifloxacin single oral dose escalation study of the effects on QTc at Cmax. The results of this study should be submitted to the Division by December 31, 2000.

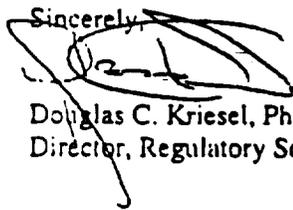


A Bristol-Myers Squibb Company

5. Bristol-Myers Squibb will conduct a comparison study of the effects of gatifloxacin, ciprofloxacin, clarithromycin, and sparfloracin on QTc at Cmax. The results of this study should be submitted to the Division by December 31, 2000.
6. The pharmacokinetic studies described in items 4 and 5 should include equal numbers of men and women over a broad range of ages (≥ 18 years; including geriatric patients).
7. Bristol-Myers Squibb should repeat the rat oral and IV-teratology studies using adequate high dose levels. The results of this study should be submitted to the Division by December 31, 2000.

If you have any questions regarding this submission, please contact me at (203) 677-6883.

Sincerely,



Douglas C. Kriesel, Ph.D.
Director, Regulatory Science

APPEARS THIS WAY
ON ORIGINAL



Bristol-Myers Squibb Company

U.S. Pharmaceutical Group

P.O. Box 4500 Princeton, NJ 08543-4500

609 897-2238 Fax: 609 897-6004

kmeriwet@uscmail.bms.com

Kathleen Meriwether
Senior Director
Regulatory Services

December 17, 1999

Via Facsimile

Ms. Laurie Bernato
Regulatory Project Manager
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: **TEQUIN™ (gatifloxacin) Tablets (NDA #21-061)**
TEQUIN™ (gatifloxacin) Injection (NDA #21-062)

Dear Ms. Bernato:

Enclosed is a draft press release announcing FDA approval of **TEQUIN™ (gatifloxacin)** for Dr. Joyce Korvick's review. Also enclosed is a copy of the full prescribing information which incorporates FDA comments and recommendations received as of December 16, 1999. The approval letter is expected later today and any last minute labeling changes will be incorporated into the labeling and forwarded to you.

A copy of the draft proposal and the latest version of full prescribing information was faxed to Jo Ann Spearmon, DDMAC Regulatory Review Officer, for review and comment. We have requested from Ms. Spearmon an expedited approval of the press release, and would appreciate your comments as quickly as possible also.

If you have any questions or require additional information, please call me.

Thank you in advance for your assistance.

Very truly yours,

Kathleen Meriwether

Attachments

cc: **J. Spearmon**
D. Kriesel

copy of the
draft press release

copy of the
full prescribing information
copy of the
draft proposal and the latest version of full prescribing information

and the
draft from
is your