

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-237/S-007

CORRESPONDENCE



ORIGINAL

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December 11, 1997

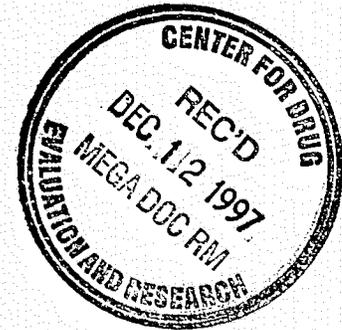
5E1-007 54
NDA SUPPL AMEND

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
S-007, Amendment 11



Dear Dr. Wilkin:

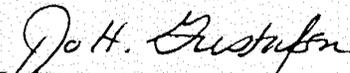
In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment provides the safety update requested by FDA on November 10, 1997.

Neither significant new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,


Jo H. Gustafson, Ph.D.

/tj

enclosure

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Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
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February 10, 1998

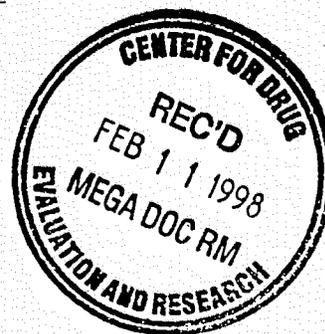
SEI-007 13L

NDA SUPPL AMEND

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
S-007, Amendment 20



Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment provides MGI PHARMA's responses and suggestions to the proposed labeling telefaxed by FDA on February 9, 1998.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

A handwritten signature in cursive script, appearing to read "Jo H. Gustafson".

Jo H. Gustafson, Ph.D.

/tj

enclosures

MGI
P H A R M A

BL

SEI-007
NDA SUPPL AMENDMENT
ORIGINAL

January 22, 1998

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Rockville, MD 20850

Via Federal Express



RE: NDA #20-237
S-007, Amendment 16

Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment provides a diskette containing the electronic version of the proposed labeling submitted on June 2, 1997 in Amendment 5 to Supplement S-007. The electronic version is in WordPerfect 6.1 for Windows 95. The document name is S007FDA.WPD. For backup, I have also put a Microsoft Office 97 version of the document on the diskette. It is named S007WORD.DOC.

This amendment also includes copies of 1) the approved March, 1997 labeling telefaxed to Dr. Blay today, 2) the June, 1997 proposed labeling printed from the WordPerfect 6.1 file, and 3) a "Compare" printout of the June label against the March label.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson
Jo H. Gustafson, Ph.D.

/tj

enclosure

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Jo H. Gustafson, Ph.D.
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January 19, 1998

NDA SUPPL AMEND
S-007 BL

Via Federal Express

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
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Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA #20-237
S-007, Amendment 15



Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment provides a second diskette containing the electronic version of the proposed labeling submitted on June 2, 1997 in Amendment 5 to Supplement S-007. The electronic version is in a Word 7.0 for Windows format. The document name is S007FDA.DOC.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson
Jo H. Gustafson, Ph.D.

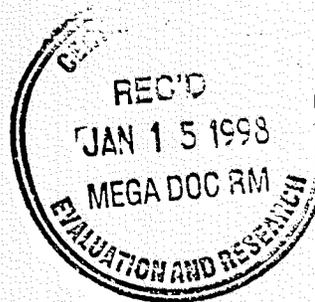
/tj

enclosure



CONFIDENTIAL

SEI-007 B.M.



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Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
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January 14, 1998

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
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Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

**RE: NDA #20-237
S-007, Amendment 14**

Dear Dr. Wilkin:

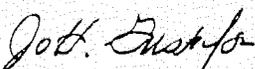
In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment is a summary of the questions raised by FDA and MGI's responses in the FDA/MGI teleconference of January 12, 1998.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,


Jo H. Gustafson, Ph.D.

/tj

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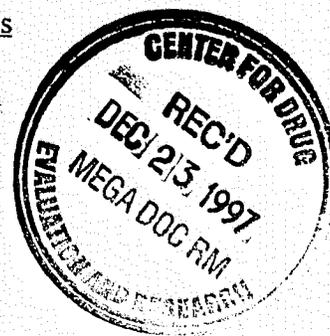
December 22, 1997

SEI-007 BM

Jo H. Gustafson, Ph.D.
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FDA/CDER/ODE V
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Rockville, MD 20850

Via Federal Express



RE: NDA #20-237
S-007, Amendment 13

Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment responds to a December 22, 1997 request from your Division.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson
Jo H. Gustafson, Ph.D.

/tj

enclosure



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SEI-007
NDA SUPPL AMENDMENT
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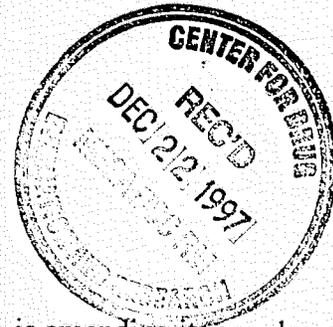
December 19, 1997

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
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Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
S-007, Amendment 12



Dear Dr. Wilkin:

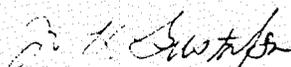
In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment addresses questions raised by FDA in the December 4th and December 15th teleconferences.

Neither significant new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,


Jo H. Gustafson, Ph.D.

/tj

enclosure

MGI

PHARMA

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SEI-007

NDA SUPPL AMENDMENT
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November 21, 1997

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
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Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
S-007, Amendment 10



Dear Dr. Wilkin:

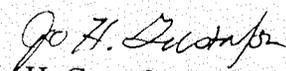
In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment responds to FDA's questions of November 14, 1997.

Neither significant new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,


Jo H. Gustafson, Ph.D.

/tj

enclosure



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381-001
NDA SUPPL AMENDMENT
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November 14, 1997

Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
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9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

RE: NDA #20-237
S-007, Amendment 9



Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment updates the supplement in accordance with FDA's final rule published in the Federal Register on July 29, 1997.

Neither significant new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,


Jo H. Gustafson, Ph.D.

/tj

enclosure



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S-007
NDA SUPPL AMENDMENT

ORIGINAL

October 30, 1997



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FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express

**RE: NDA #20-237
S-007, Amendment 8**

Dear Dr. Wilkin:

In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment responds in writing to FDA/MGI PHARMA telephone discussions regarding the laptop computer on loan to Dr. Farr to facilitate her review of this supplement.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,

Jo H. Gustafson
Jo H. Gustafson, Ph.D.

/tj

enclosures

MGI

PHARMA

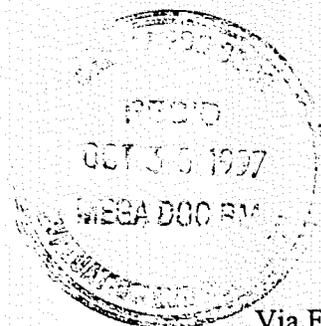
CONFIDENTIAL

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Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

October 29, 1997



SEI-007 BM
NDA SUPPL AMEND

Via Federal Express

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA #20-237
S-007, Amendment 7

Dear Dr. Wilkin:

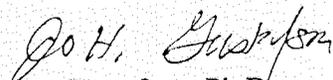
In accordance with 21 CFR 314.60(a), MGI PHARMA, INC. is amending its supplement to expand the indication to include treatment for symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome.

This amendment responds in writing to voice mail requests of October 24, 1997 from Dr. Roy Blay.

Neither new data nor a new analysis of previously submitted data is included in this amendment. Thus, per 21 CFR 314.60(a), submission of this amendment will not extend the review period of the supplement.

Please contact me if you have any questions regarding this submission.

Cordially,


Jo H. Gustafson, Ph.D.

/tj

enclosures

MGI
P H A R M A

ORIGINAL

SEI-007 SU
NDA SUPPL AMEND

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Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

October 8, 1997



Via Federal Express

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

**RE: NDA #20-237, Supplement S-007
General Correspondence**

Dear Dr. Wilkin:

The purpose of this general correspondence is to state MGI PHARMA's understandings and intentions with respect to a safety update for supplement S-007 currently under review in your Division for the treatment of symptoms of dry mouth and dry eyes in patients with Sjögren's syndrome. At the October 11, 1996 "pre-NDA" meeting for this supplement, FDA requested long-term safety data on at least 300 patients for six months, and 100 patients for a full year of treatment. FDA allowed for safety data from studies designed for different indications if there were comparable drug level exposures, but expected approximately half of the long-term safety data to be from Sjögren's patients.

For reasons stated in the following paragraphs, MGI PHARMA believes that no safety update is required for this supplement as per 21 CFR 314.71(b) in which: "the information required in the supplement is limited to that needed to support the change" requested in the supplement.

The February 11, 1997 supplement included an interim safety report on the open-label maintenance study (protocol 92-03). This report included at least 3 months of safety information on 431 of 437 patients. The total patient numbers in the report exceeded the criteria for review set at the October meeting, c.f. table on Page 19 of Volume 132 in Supplement S-007 (copy enclosed).

Since that submission, additional exposure information has been obtained for 9 patients through Month 6 (from 361 to 370 patients) and for 48 patients through Month 12 (from 245 to 293). The last patient completed study participation April, 1997. Consistent with information in the February 11, 1997 supplement, no serious drug-related adverse

experiences have been reported to MGI PHARMA. The largest changes in the incidence of adverse experiences were an increase in reported flu (from 25.0% to 34.4%), sweating (from 45.3% to 49.5%), and conjunctivitis (from 2.8% to 6.1%). None of these data will materially alter the conclusions concerning the safety of oral pilocarpine in the original integrated summary of safety information (submitted in February 11, 1997 as the Interim Report) for use in patients with Sjögren's syndrome.

MGI PHARMA does not intend to use the results of this study to modify the proposed package insert for Salagen® Tablets.

Given the above information, MGI PHARMA believes that per 21 CFR 314.81(b)(2)(vi)(b), the appropriate timing for submission of the final study information is in the upcoming 1998 Salagen® Tablet NDA annual report for the period March 23, 1997 through March 22, 1998.

Therefore, MGI PHARMA anticipates submission of the final study safety information in the annual report as a postapproval submission.

Please contact me if you have any questions regarding this analysis and intended plan of action.

Cordially,


J. H. Gustafson, Ph.D.
Director, Regulatory Affairs

/tj

Enclosures

July 31, 1997

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
Dental Drug Products, HFD-540
Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

Via Federal Express



**RE: NDA #20-237, S-007
Request for Meeting**

Dear Dr. Wilkin:

By this letter, MGI PHARMA is requesting a meeting in mid-to-late September to learn of any issues that have arisen by early September in review of this supplement. MGI requests that at that meeting, FDA inform MGI of the general progress and status of S-007, and that FDA advise MGI of any issues that have been identified by that time and have not yet already been communicated to MGI.

While that is the purpose of the 90-day conference identified under 21 CFR 314.102(c), MGI PHARMA believes that scheduling of that conference shortly into the eighth month is appropriate, based on Dr. Lumpkin's identification of FDA review process events comparable to EU review process events.

On June 25, 1997, at the DIA meeting in Montreal, Dr. Lumpkin identified that the EU event process completion of first CPMP review and assessment, a process to be completed within 210 days of the application, is comparable to completion of an FDA Division Director review with any advisory committee input.

While MGI PHARMA hopes to receive an action letter in September, c.f. MGI's letter of June 17, 1997 to NDA #20-237, MGI PHARMA believes that if an action cannot be completed by that time, a meeting to identify all outstanding issues shortly after completion of Division Director review will facilitate the overall timing of the review process. MGI PHARMA may be able to identify areas within the supplement or the NDA file which address questions FDA might have.

Since the intent of the meeting is for MGI PHARMA to hear the issues identified, MGI PHARMA will not be making a formal presentation. A list of the proposed meeting attendees and the proposed agenda follows.

Cordially,



Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs

/cs

Enclosures

cc: Dr. M. Haffner
Mr. J. Morrison

ORIGINAL



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June 17, 1997



Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs
Direct: 612-939-4665

Jonathan Wilkin, M.D., Director
FDA/CDER/ODE V
Division of Dermatologic and
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Building 2, Second Floor, Room N203
9201 Corporate Boulevard
Rockville, MD 20850

SUPPL NEW CORRERO

Via Federal Express

RE: Review Classification for NDA 20-237, S-007

Dear Dr. Wilkin:

On behalf of MGI PHARMA, INC., I thank you very much for the opportunity to meet with you and your associates regarding the review classification for this supplement. We understand that the Division's position is that supplement S-007 does not meet the MAPP definition of priority review because use of Salagen® Tablets was not compared against use of OTC products. We respectfully disagree with that position because we believe that the significant improvement demonstrated in our pivotal studies by Salagen® Tablets with concurrent prn use of mouth and eye comfort products indicates "significant improvement" over these coping products alone.

However, given that we are now in the fourth month of review, we know that the Division cannot realistically switch from a standard review classification to a priority review classification, given the implications of such a switch on PDUFA obligations. Therefore, we would like very much for you to consider an internal review assignment of eight months from submission.

MGI PHARMA believes this is a realistic timeframe for several reasons. We note that Dr. Chambers has carried his review to the point of response sufficient for an action letter.

This is a relatively straightforward supplement. All chemistry items were reviewed and resolved in advance of the submission. In addition, the pre-NDA meeting and follow-up teleconferences produced agreement on the presentation of the clinical trial data.

The supplement is extremely focused with two pivotal trials with highly significant results. In this regard, as indicated by Dr. Chambers' comments during our meeting, significant review has already occurred. The trials showed a safety profile consistent with the safety profile in the current labeling. Therefore, review of the labeling can also be focused.

Also, as you observed at your meeting, MGI PHARMA has made every effort to facilitate the review process with rapid responses to all FDA questions and requests. We stand ready to address any further requests or responses. In that light, I will be contacting our project manager to identify any items early on so that we may address them as quickly as possible.

Cordially,



Jo H. Gustafson, Ph.D.
Director, Regulatory Affairs

/tj

cc: J. Morrison
P. Vaccari