

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-101

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**



NDA 22-101

NEXIUM® (esomeprazole magnesium)

Delayed-Release Granules for Oral Suspension

New Drug Application

1.3.5.1 Patent Information

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**
*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

22-101

NAME OF APPLICANT / NDA HOLDER

AstraZeneca LP

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

NEXIUM® (esomeprazole magnesium) Delayed-Release Capsules

ACTIVE INGREDIENT(S)

Esomeprazole magnesium

STRENGTH(S)

20 mg and 40 mg of Esomeprazole

DOSAGE FORM

oral

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number
4,738,974

b. Issue Date of Patent
4/19/1988

c. Expiration Date of Patent
4/19/2007

d. Name of Patent Owner
AB Hässle

Address (of Patent Owner)
SE-431 83

City/State
Möndal, Sweden

ZIP Code
SE-431 83

FAX Number (if available)

Telephone Number
001146 31 7761000

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code
19803

FAX Number (if available)

Telephone Number
(800) 456-3669

E-Mail Address (if available)

Vice President, Policy, Legal & Scientific
Affairs and General Counsel
AstraZeneca Pharmaceuticals LP

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No*

* Certain claims may cover at least one additional polymorph in addition to claiming the drug substance of the pending NDA, amendment or supplement, but the patent is not being listed on that basis.

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

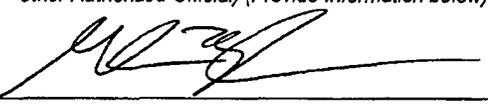
4.2 Patent Claim Number (as listed in the patent) 9, 10, 12, 13, 14 and 16 Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
See NEXIUM Delayed Release Capsules and Granules in Label at DESCRIPTION, DOSAGE FORMS AND STRENGTHS, USE IN SPECIFIC POPULATIONS (incl. Pediatric Use), CLINICAL PHARMACOLOGY (incl. Pediatric Use), INDICATIONS AND USAGE, Information for Patients DOSAGE AND ADMINISTRATION.

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6. Declaration Certification	
<p>6.1 <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i></p> <p>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</p>	
<p>6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)</p> 	<p>Date Signed</p> <p style="text-align: center;">9/14/06</p>
<p>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</p>	
<p>Check applicable box and provide information below.</p>	
<p><input type="checkbox"/> NDA Applicant/Holder</p> <p><input type="checkbox"/> Patent Owner</p>	<p><input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official</p> <p><input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official</p>
<p>Name Glenn M Engelmann, Vice President, Policy, Legal & Scientific Affairs and General Counsel</p>	
<p>Address 1800 Concord Pike</p>	<p>City/State Wilmington, DE</p>
<p>ZIP Code 19803</p>	<p>Telephone Number (302) 886-3000</p>
<p>FAX Number (if available) (302) 886-1578</p>	<p>E-Mail Address (if available) glenn.engelmann@astrazeneca.com</p>
<p>The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Food and Drug Administration CDER (HFD-007) 5600 Fishers Lane Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	

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NEXIUM® Delayed-Release Granules for Oral Suspension

ACTIVE INGREDIENT(S)

Esomeprazole magnesium

STRENGTH(S)

10 mg of Esomeprazole

DOSAGE FORM

oral

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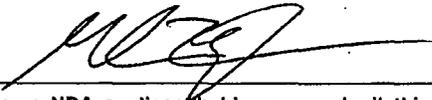
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6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



9/11/06

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Glenn M Engelmann, Vice President, Policy, Legal & Scientific Affairs and General Counsel

Address

1800 Concord Pike

City/State

Wilmington, DE

ZIP Code

19803

Telephone Number

(302) 886-3000

FAX Number (if available)

(302) 886-1578

E-Mail Address (if available)

glenn.engelmann@astrazeneca.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

EXCLUSIVITY SUMMARY

NDA # 22-101

SUPPL #

HFD # 180

Trade Name Nexium

Generic Name esomeprazole magnesium

Applicant Name AstraZeneca

Approval Date, If Known February 27, 2008

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505 (b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

Yes

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 21-153 Delayed Release Capsules (esomeprazole magnesium)
NDA# 21-957 Delayed Release Oral Suspension (esomeprazole magnesium)
NDA# 21-689 IV injection (esomeprazole sodium)

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Approval based on demonstrated bioavailability (Study 9614C00099) supported by the safety (Study D9614C00097).

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Study 9614C00099 and Study D9614C00097

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1
IND # 53,733 YES ! NO
! Explain:

Investigation #2
IND # 53,733 YES ! NO
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES
Explain:

!
!
! NO
! Explain:

Investigation #2

YES
Explain:

!
!
! NO
! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO

If yes, explain:

Name of person completing form: Chantal Phillips
Title: Regulatory Project Manager
Date: February 27, 2008

Name of Office/Division Director signing form: Joyce Korvice, M.D., M.P.H.
Title: Deputy Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

Chantal N. Phillips
2/27/2008 03:28:25 PM
CSO

Joyce Korvick
2/27/2008 05:20:23 PM
MEDICAL OFFICER

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 22-101 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: December 27, 2007 PDUFA Goal Date: February 27, 2008

HFD 180 Trade and generic names/dosage form: Nexium (esomeprazole magnesium) Delayed-Release Granules for Oral Suspension

Applicant: AstraZeneca Therapeutic Class: 8015664

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- Yes. Please proceed to the next question.
 No. PREA does not apply. Skip to signature block.

* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): _____

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 2

Indication #1: Short term treatment of GERD

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
 No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
 No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
 Disease/condition does not exist in children
 Too few children with disease to study
 There are safety concerns
 Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min _____ kg _____ mo. 0 yr. <1 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: Clinical studies are ongoing

Date studies are due (mm/dd/yy): 12/31/08

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. 1-11 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

This submission is a partial response to Written Request

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

NDA 22-101

Page 3

This page was completed by:

{See appended electronic signature page}

Chantal Phillips
Regulatory Project Manager

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH
STAFF at 301-796-0700**

(Revised: 10/10/2006)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: Healing of Erosive Esophagitis

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
- No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver X Deferred ___ Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min _____ kg _____ mo. 0 yr. <1 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: clinical studies are ongoing

Date studies are due (mm/dd/yy): 12/31/08

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. 1-11 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

This submission is a partial response to Written Request

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Chantal Phillips
Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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/s/

Chantal N. Phillips
2/7/2008 10:25:11 AM



NDA 22-101

NEXIUM® (esomeprazole magnesium)

Delayed-Release Granules for Oral Suspension

New Drug Application

1.3.3 Debarment Certification

NEXIUM® (esomeprazole magnesium) Delayed-Release Granules for Oral Suspension
NDA 22-101: New Drug Application

ITEM 16 DEBARMENT CERTIFICATION

Re: NDA 22-101

**NEXIUM® (esomeprazole magnesium) Delayed-Release Granules for Oral Suspension
Debarment Certification Statement**

In response to the requirements of the Generic Drug Enforcement Act of 1992, I hereby certify on behalf of AstraZeneca LP (AstraZeneca), that we did not use and will not use in connection with this New Drug Application for NEXIUM® (esomeprazole magnesium) Delayed-Release Granules for Oral Suspension, NDA 22-101 (Study Number D9612C00032), the services of any person in any capacity debarred under section 306 (a) or (b).

Sincerely,



Donna M. Dea, Vice President
Regulatory Affairs
AstraZeneca LP

ACTION PACKAGE CHECKLIST

Application Information		
BLA # NDA # 22-101	BLA STN# NDA Supplement #	If NDA, Efficacy Supplement Type
Proprietary Name: Nexium Established Name: esomeprazole magnesium Dosage Form: Delayed-Release Granules for Oral Suspension		Applicant: AstraZeneca
RPM: Chantal Phillips		Division: Gastroenterology Products Phone # 301-796-2259
NDAs: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) (A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)		505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): Provide a brief explanation of how this product is different from the listed drug. <input type="checkbox"/> If no listed drug, check here and explain: Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct. <input type="checkbox"/> Confirmed <input type="checkbox"/> Corrected Date:
❖ User Fee Goal Date ❖ Action Goal Date (if different)		February 27, 2008
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions (<i>specify type and date for each action taken</i>)		<input type="checkbox"/> None AE: July 27, 2007
❖ Advertising (<i>approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (<i>indicate dates of reviews</i>)		<input checked="" type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

<p>❖ Exclusivity</p>	
<ul style="list-style-type: none"> • NDAs: Exclusivity Summary (approvals only) (<i>file Summary in Administrative Documents section</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> • Is approval of this application blocked by any type of exclusivity? <ul style="list-style-type: none"> • NDAs/BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> • NDAs: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> • NDAs: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> • NDAs: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires: <input type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA # and date exclusivity expires: <input type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA # and date exclusivity expires:
<p>Patent Information (NDAs and NDA supplements only)</p>	
<ul style="list-style-type: none"> • Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> • Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. • [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii) <input type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> • [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). (<i>If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews).</i>) • [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. <p>Answer the following questions for each paragraph IV certification:</p> <p>(1) Have 45 days passed since the patent owner’s receipt of the applicant’s</p>	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified <input type="checkbox"/> Yes <input type="checkbox"/> No

<p>within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.</i></p>	
Summary Reviews	
❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review)	2/27/08
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)	NA
Labeling	
❖ Package Insert	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	February 27, 2008
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	NA
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	Sept. 27, 2006
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	Prevacid Oral Suspension
❖ Patient Package Insert	
<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	February 27, 2008
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	NA
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	September 27, 2006
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
❖ Medication Guide	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling) 	
❖ Labels (full color carton and immediate-container labels)	
<ul style="list-style-type: none"> • Most-recent division-proposed labels (only if generated after latest applicant submission) 	February 27, 2008 in action letter
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	Dec.27, 2007
❖ Labeling reviews and minutes of any labeling meetings (indicate dates of reviews and meetings)	<input checked="" type="checkbox"/> DMETS 12/22/06, 2/27/08 <input type="checkbox"/> DSRCS <input checked="" type="checkbox"/> DDMAC July 25, 2007 <input checked="" type="checkbox"/> SEALD 12/14/06, 2/11/08 <input type="checkbox"/> Other reviews <input type="checkbox"/> Memos of Mtgs

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> • Facility review (<i>indicate date(s)</i>) • Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>) 	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed
Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	June 5, 2007
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	NA
❖ Nonclinical inspection review Summary (DSI)	<input checked="" type="checkbox"/> None requested
Clinical Information	
❖ Clinical review(s) (<i>indicate date for each review</i>)	July 23, 2007
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	See MO review dated 7/23/07
❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)	See MTL review dated Feb. 8, 2008
❖ Risk Management Plan review(s) (including those by OSE) (<i>indicate location/date if incorporated into another review</i>)	NA
❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
• Clinical Studies	
• Bioequivalence Studies	
• Clin Pharm Studies	
❖ Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None July 20, 2007
❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None July 3, 2007

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/s/

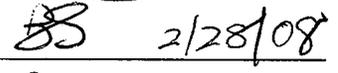
Chantal N. Phillips
2/29/2008 10:29:39 AM

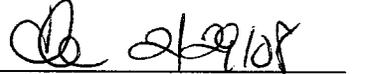
NDA SUPPLEMENT ACTION PACKAGE CHECKLIST SIGN-OFF SHEET

Application Information			
NDA 22-101			
Drug: Nexium (esomeprazole magnesium) For Delayed – Release Oral Suspension		Applicant: AstraZeneca	
RPM: Chantal Phillips		HFD-180	Phone # 301-796-2259
Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	
❖ Application Classifications:			
• Review priority			<input type="checkbox"/> Standard <input checked="" type="checkbox"/> Priority
• Chem class (NDAs only)			3
• Other (e.g., orphan, OTC)			
❖ User Fee Goal Dates			2/27/08

Reviewers Sign Off List

Hugo Gallo-Torres, M.D., Ph.D., P.N.S., Medical Team Leader  02/28/08

Brian Strongin, R.Ph., M.B.A., Supervisory Project Manager  2/28/08

Joyce Korvick, M.D., M.P.H., Deputy Division Director  2/29/08



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-101

AstraZeneca
Attention: George Kummeth
Global Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803

Dear Mr. Kummeth:

We acknowledge receipt on December 27, 2007 of your December 27, 2007, resubmission to your supplemental new drug application for Nexium (esomeprazole magnesium) For Delayed-Release Oral Suspension, 10mg.

We consider this a complete, class 1 response to our July 27, 2007, action letter. Therefore, the primary user fee goal date is February 27, 2008.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have submitted pediatric studies with this application. Once the review of this application is complete we will notify you whether you have fulfilled the pediatric study requirement for this application.

If you have any questions, call me at (301) 796-2259.

Sincerely,

{See appended electronic signature page}

Chantal Phillips, LCDR, B.S.N.
Regulatory Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Chantal N. Phillips
1/16/2008 04:18:29 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Mail: ODS		FROM: Division of Gastroenterology Products Chantal Phillips, RPM		
DATE January 16, 2008	IND NO.	NDA NO. 22-101	TYPE OF DOCUMENT Class 1 Response	DATE OF DOCUMENT December 27, 2007
NAME OF DRUG Nexium		PRIORITY CONSIDERATION 2 month review	CLASSIFICATION OF DRUG PPI	DESIRED COMPLETION DATE PDUFA: 2/27/08
NAME OF FIRM:				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> * RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS:				
<p>This is a complete response to our approvable letter sent on July 27, 2007. An approvable letter was sent due to pending review of cardiac safety related to SOPRAN/LOTUS studies submitted by sponsor. Agreements regarding package insert were reached. Recommendations from DMETS regarding the carton label and foil insert were incorporated into the AE letter. Sponsor has resubmitted revised carton label and foil packet label that appear to meet the recommendations originally suggested by DMETS review dated 12/22/06 by Kristina Arnwine. We are seeking your input and expertise on whether the revised labeling meets DMETS recommendations.</p> <p>Submission in EDR, dated 12/27/07: <u>\\CDSESUB1\NONECTD\N22101\N_000\2007-12-27</u></p> <p>Thank you.</p>				
SIGNATURE OF REQUESTER Chantal Phillips		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

Chantal N. Phillips
1/16/2008 02:59:48 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-101

AstraZeneca
Attention: George Kummeth
Global Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Kummeth:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium (esomeprazole magnesium) Delayed-Release Granules for Oral Suspension.

We also refer to the teleconference that occurred on July 27, 2007, between the FDA representatives, Dr. Joyce Korvick and Chantal Phillips and AstraZeneca representatives, George Kummeth, Dr. Doug Levine, and Mersedeh Miraliakbari. We discussed the action for this submission as well as the unresolved labeling issue related to the "Initial U.S. Approval date of 1989" for Nexium.

Since this teleconference, we have sought internal clarification with the Office of Chief Counsel and they have recommended the following be placed in the label:

In the Highlights section, the approval date should be listed as:

Initial U.S. Approval: 1989 (omeprazole)

Under Section 11: Description (first paragraph), you may add the approval date of esomeprazole by using the text in the example provided below:

Esomeprazole is the S-isomer of omeprazole, which is a mixture of the S- and R- isomers. (Initial U.S. Approval of esomeprazole magnesium: 2001. Its chemical name is [insert chemical name]. The structural formula is:

[Insert chemical structure here]

If you have any questions, call Chantal Phillips, Regulatory Project Manager, at 301-796-2259.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Joyce Korvick
12/18/2007 10:00:51 AM

MEMORANDUM OF TELECON

DATE: July 27, 2007

APPLICATION NUMBER: NDA 22-101

BETWEEN:

Name: George Kummeth, Global Director
Dr. Doug Levine
Mersedeh Miraliakbari
Phone: (302) 885-8415
Representing: AstraZeneca

AND

Name: Dr. Joyce Korvick, Deputy Director
Chantal Phillips, Regulatory Project Manager
DIVISION NAME, HFD-180

SUBJECT: Unresolved Labeling and Action for NDA 22-101

The sponsor accepted all FDA revisions to the label for NDA 22-101 sent by correspondence on July 26, 2007, except for the "Initial U.S. Approval date of 1989", recommended by the SEALD Review Team. The sponsor states that this creates ambiguity since Nexium was approved in 2001.

The FDA understands the concerns expressed by the sponsor but stated that this issue cannot be resolved today.

The FDA confirmed receipt of the final report from July 25, 2007 regarding the SOPRAN and LOTUS studies submitted to NDA 21-153 and informed sponsor that in light of this ongoing review for cardiac safety, the FDA is taking an approvable action on NDA 22-101. The Pediatric team was consulted in this decision and agrees with this action due to the unknown cardiac safety involving Nexium.

The FDA cannot approve this NDA until the review has been completed on the final SOPRAN and LOTUS studies submitted on July 25, 2007. The FDA will notify the sponsor upon completion of this review so that NDA 22-101 may be resubmitted. The labeling for NDA 22-101 may or may not need to be revised regarding cardiac safety.

In the interim, the FDA will also seek internal clarification regarding the unresolved issue pertaining to the date of "Initial U.S. Approval" in the Highlights section of the label and the Sponsor states that they will do the same.

Upon completion of reviewing the SOPRAN and LOTUS studies, the FDA would like the sponsor to resubmit NDA 22-101 as a 2 month review, with the labeling identical to the version sent to the sponsor on July 26, 2007. The sponsor understands and respects the FDA's decision regarding this action and does not anticipate communications regarding this decision above the Division level.

Chantal Phillips, LCDR
Regulatory Project Manager

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/s/

Chantal N. Phillips
7/30/2007 03:02:02 PM
CSO



NDA 22-101

INFORMATION REQUEST LETTER

AstraZeneca
Attention: George Kummeth
Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Kummeth:

Please refer to your September 27, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium (esomeprazole magnesium) 10 mg.

We are reviewing the Clinical Pharmacology section of your submission and have the following comments and information requests regarding analytical reports. We request a prompt written response in order to continue our evaluation of your NDA.

Study No. D9614C00099:

You indicated in the section "5.5.2.3 Drug concentration measurements" of the individual study report (p. 29 of 659) that the plasma concentrations of esomeprazole and the sulphone metabolite were determined at DMPK & Bioanalytical Chemistry, AstraZeneca R&D Mölndal, Sweden, using _____, liquid chromatography and UV detection according to method No. BA-222 (AstraZeneca R&D Mölndal Report No. Q-21178 2002)."

b(4)

Study No. D9612C00032:

You indicated in the section "5.5.2.3 Drug concentration measurements" of the individual study report (p. 26 of 464) that samples for determination of esomeprazole in plasma were analyzed at _____ on behalf of DMPK & Bioanalytical Chemistry, AstraZeneca R&D Mölndal, Sweden using _____ liquid chromatography and UV-detection according to method no. AS M-002 version 3 (_____ implementation of AstraZeneca method no. BA-222) and the bioanalytical results are presented in the bioanalytical study validation report 41312-0546-01. The method validation is documented in the report PMC-9441.

b(4)

NDA 22-101

Study No. **SH-NEC-0001**:

You indicated in the section "**5.5.2.3 Drug concentration measurements**" of the individual study report (p. 35 of 852) that the plasma concentrations of esomeprazole, the sulphone metabolite and the 5-hydroxy metabolite were determined at DMPK & Bioanalytical Chemistry AstraZeneca R&D Mölndal, Sweden, using liquid chromatography and mass spectrometric detection according to method No. BA-390. The limit of quantification (LOQ) was 5.0 nmol/L for esomeprazole, the sulphone metabolite and the 5-hydroxy metabolite. The bioanalytical study is documented in report 41312-0634-01. The method validation is documented in report 41312-0064-01.

b(4)

In order to complete the review of NDA 22-101, please provide us with the locations (page and volume numbers) of these analytical reports in your NDA submitted on September 27, 2006.

If you have any questions, call Chantal Phillips, Regulatory Project Manager, at 301-796-2259.

Sincerely,

{See appended electronic signature page}

Brian Strongin, R.Ph., M.B.A.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Brian Strongin
5/11/2007 12:29:14 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-101

INFORMATION REQUEST LETTER

AstraZeneca LP
Attention: George Kummeth
Global Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Kummeth:

Please refer to your September 27, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium (esomeprazole magnesium) Delayed-Release Granules, 10mg.

We also refer to your submission dated February 1, 2007.

We are reviewing the Statistical section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. For the three variables Heartburn, Acid Regurgitation, and Epigastric Pain, instead of using the average of the seven data points from the 8th week, please perform the following:
 - a) Paired t-tests using the data point from the 7th day of the 8th week and one data point at Baseline to explore if patients improved from Baseline assessed at the final date of the treatment.
 - b) Please submit the data set and programs used in the exploratory analyses.

If you have any questions, call Chantal Phillips, Regulatory Project Manager, at 301-796-2259.

Sincerely,

{See appended electronic signature page}

Brian Strongin, R.Ph., M.B.A.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Brian Strongin
2/22/2007 02:33:31 PM

MEMORANDUM OF TELECON

DATE: January 29, 2007

APPLICATION NUMBER: NDA 22-101

BETWEEN:

Name: Mersedeh Miraliakbari, Associate Director, Regulatory Affairs
Barry Traxler, Principal statistician
Peter Barker, PhD, Sr. Statistician
Yibin Rong, Principal programmer
Phone: (302) 885-4317
Representing: AstraZeneca

AND

Name: Chantal Phillips, Project Manager
Kristen Everett, Project Manager
Wen Jen Chen, Ph.D., Statistician
Division of Gastroenterology Products, HFD-180

SUBJECT: Request for and clarification of statistical information for NDA 22-101

Dr. Wen Jen Chen requested a telephone conference with the statisticians from AstraZeneca in order to clarify and request data for NDA 22-101 submitted on September 27, 2006. Dr. Wen Jen Chen asked the following bolded questions and the sponsor's responses follow.

In the analyses for the three variables Heartburn, Acid Regurgitation, and Epigastric Pain reported by the parents/guardians; did you use the average of the 7 data points for the Final Visit and one data point at Baseline?

Yes, we did use the average of the 7 data points for the assessment of symptoms in the final week. The baseline assessment of GERD-related symptoms was captured on a single case report form with a 72-hour recall period specified. On-treatment symptoms were to be recorded on a daily basis, via the parent/guardian telephoning the IVRS (Interactive Voice Response System).

Please submit the information you provided regarding this question during the T-con and also provide the 7 individual data points for each of the three variables from the Final Visit for both ITT and PP populations.

Sponsor agreed to submit.

Please submit the individual Final Visit data together with the LA Classification data. The SAS format code can be submitted by separate file.

Sponsor agreed to submit.

In the analyses for the physician assessment score, did you compare the ordinal categories for the Baseline versus the Final Visit using Cochran-Mantel-Haensel method for each of the four treatment groups?

Yes, the Cochran-Mantel-Haensel test was used to compare the ordinal categories for the baseline versus the final visit global assessment score, and no stratification variable was specified; this reduces to the Mantel-Haensel test in this situation. No formal comparisons between the treatment groups were planned or performed.

Please submit the information you provided regarding this question during the T-con.

Sponsor agreed to submit.

Chantal Phillips, LCDR, BSN
Regulatory Project Manager

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/s/

Chantal N. Phillips
2/12/2007 04:10:32 PM
CSO

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 22-101 Supplement # Efficacy Supplement Type SE-

Proprietary Name: Esomeprazole Magnesium
Established Name: Nexium
Strengths: 10mg

Applicant: Astra Zeneca LP
Agent for Applicant (if applicable):
Date of Application: Sept 27, 2006
Date of Receipt: Sept 27, 2006
Date clock started after UN:
Date of Filing Meeting: October 23, 2006
Filing Date: November 26, 2006
Action Goal Date (optional): May 27, 2007

User Fee Goal Date: July 27, 2007

Indication(s) requested:

Type of Original NDA: (b)(1) (b)(2)
AND (if applicable)
Type of Supplement: (b)(1) (b)(2)

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application or efficacy supplement is a (b)(2), complete Appendix B.

Review Classification: S P
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 5
Other (orphan, OTC, etc.)

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee Status: Paid Exempt (orphan, government)
Waived (e.g., small business, public health)

NOTE: If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required by contacting the User Fee staff in the Office of Regulatory Policy. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the User Fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2)

application? YES NO
 If yes, explain:

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

• Does another drug have orphan drug exclusivity for the same indication? YES NO

• If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

• Is the application affected by the Application Integrity Policy (AIP)? YES NO
 If yes, explain:

• If yes, has OC/DMPQ been notified of the submission? YES NO

• Does the submission contain an accurate comprehensive index? YES NO
 If no, explain:

• Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.

• Submission complete as required under 21 CFR 314.50? YES NO
 If no, explain:

• Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES

2. This application is an eNDA or combined paper + eNDA YES
 This application is: All electronic Combined paper + eNDA
 This application is in: NDA format CTD format
 Combined NDA and CTD formats

Does the eNDA, follow the guidance? YES NO
 (<http://www.fda.gov/cder/guidance/2353fnl.pdf>)

If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format?

Additional comments:

3. This application is an eCTD NDA. YES
If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments:

- Patent information submitted on form FDA 3542a? YES NO
- Exclusivity requested? YES, 3 Years NO
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

- Correctly worded Debarment Certification included with authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge . . ."

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES NO
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES NO
- Is this submission a partial or complete response to a pediatric Written Request? YES NO

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES NO
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)

NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.

- Field Copy Certification (that it is a true copy of the CMC technical section) YES NO
- PDUFA and Action Goal dates correct in tracking system? YES NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.

- List referenced IND numbers: IND 53,733

- Are the trade, established/proper, and applicant names correct in COMIS? YES NO
If no, have the Document Room make the corrections.

- End-of-Phase 2 Meeting(s) Date(s) _____ NO
If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s) Date(s) _____ NO
If yes, distribute minutes before filing meeting.

- Any SPA agreements? Date(s) _____ NO

If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES NO
If no, request in 74-day letter.
- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
Was the PI submitted in PLR format? YES NO

If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:
- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES NO
- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES NO
- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?
N/A YES NO
- Risk Management Plan consulted to OSE/IO? N/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA YES NO

If Rx-to-OTC Switch or OTC application:

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES NO
- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? NA YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to EA officer, OPS? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team? NA YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: October 23, 2006

NDA #: 22-101

DRUG NAMES: Nexium Delayed-Release Granules

APPLICANT: Astra Zeneca LP

BACKGROUND:

This NDA provides for a new delayed-release granules for oral suspension formulation of Nexium and revisions to the pediatric section of the package insert, adding information regarding the use of Nexium in patients aged 1-11 years for the short-term treatment of GERD and healing of erosive esophagitis.

ATTENDEES: Dr. Wen Yi-Gao, Marie Kowblansky, Dr. Jasti Choudary, Dr. Hugo Gallo-Torres, Dr. Ke Zhang, Milton Sloan, Dr. Brian Harvey, Dr. Stella Grosser, Dr. Suliman Al-Fayoumi, Tanya Clayton, Chantal Phillips

ASSIGNED REVIEWERS (including those not present at filing meeting): Dr. Wen Yi-Gao, Wen Chen, Milton Sloan, Sue Chih Lee, Ke Zhang

Discipline/Organization

Reviewer

Medical:	Dr. Hugo Gallo-Torres
Secondary Medical:	Dr. Wen Yi-Gao
Statistical:	Wen Jen Chen
Pharmacology:	Dr. Ke Zhang
Statistical Pharmacology:	
Chemistry:	Milton Sloan
Environmental Assessment (if needed):	Bai Nguyen
Biopharmaceutical:	Dr. Tien-Mien Chen
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	
OPS:	
Regulatory Project Management:	Chantal Phillips
Other Consults:	Pediatrics, DDMAC, DMETS

Per reviewers, are all parts in English or English translation? YES NO
If no, explain:

CLINICAL FILE REFUSE TO FILE

- Clinical site audit(s) needed? YES NO
If no, explain: Dr. Hugo Gallo-Torres stated it was not needed.
- Advisory Committee Meeting needed? YES, date if known _____ NO
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

	N/A	<input checked="" type="checkbox"/>	YES	<input type="checkbox"/>	NO	<input type="checkbox"/>
CLINICAL MICROBIOLOGY	N/A	<input checked="" type="checkbox"/>	FILE	<input type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
STATISTICS	N/A	<input type="checkbox"/>	FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
BIOPHARMACEUTICS			FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
• Biopharm. study site audits(s) needed?			YES	<input type="checkbox"/>	NO	<input checked="" type="checkbox"/>
PHARMACOLOGY/TOX	N/A	<input type="checkbox"/>	FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
• GLP audit needed?			YES	<input type="checkbox"/>	NO	<input checked="" type="checkbox"/>
CHEMISTRY			FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
• Establishment(s) ready for inspection?			YES	<input type="checkbox"/>	NO	<input type="checkbox"/>
• Sterile product?			YES	<input type="checkbox"/>	NO	<input checked="" type="checkbox"/>
If yes, was microbiology consulted for validation of sterilization? NA			YES	<input type="checkbox"/>	NO	<input type="checkbox"/>

ELECTRONIC SUBMISSION:
Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:
(Refer to 21 CFR 314.101(d) for filing requirements.)

- The application is unsuitable for filing. Explain why:
- The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.
 - No filing issues have been identified.
 - Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.
2. If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
3. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
4. If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)
5. Convey document filing issues/no filing issues to applicant by Day 74.

Chantal Phillips
Regulatory Project Manager

Appendix A to NDA Regulatory Filing Review

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original application is likely to be a 505(b)(2) application if:

- (1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
- (2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),
- (2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and.
- (3) All other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the

original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),

- (2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or
- (3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's Office of Regulatory Policy representative.

**Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications**

1. Does the application reference a listed drug (approved drug)? YES NO

If "No," skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):
3. Is this application for a drug that is an "old" antibiotic (as described in the draft guidance implementing the 1997 FDAMA provisions? (Certain antibiotics are not entitled to Hatch-Waxman patent listing and exclusivity benefits.) YES NO

If "Yes," skip to question 7.

4. Is this application for a recombinant or biologically-derived product? YES NO

If "Yes" contact your ODE's Office of Regulatory Policy representative.

5. The purpose of the questions below (questions 5 to 6) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.
- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved? YES NO

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

If "No," to (a) skip to question 6. Otherwise, answer part (b and (c)).

- (b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval? YES NO
- (c) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES NO

If "Yes," (c), list the pharmaceutical equivalent(s) and proceed to question 6.

If "No," to (c) list the pharmaceutical equivalent and contact your ODE's Office of Regulatory Policy representative.

Pharmaceutical equivalent(s):

6. (a) Is there a pharmaceutical alternative(s) already approved? YES NO

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

If "No," to (a) skip to question 7. Otherwise, answer part (b and (c)).

- (b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval? YES NO

- (c) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES NO

If "Yes," to (c), proceed to question 7.

NOTE: If there is more than one pharmaceutical alternative approved, consult your ODE's Office of Regulatory Policy representative to determine if the appropriate pharmaceutical alternatives are referenced.

If "No," to (c), list the pharmaceutical alternative(s) and contact your ODE's Office of Regulatory Policy representative. Proceed to question 7.

Pharmaceutical alternative(s):

7. (a) Does the application rely on published literature necessary to support the proposed approval of the drug product (i.e. is the published literature necessary for the approval)? YES NO

If "No," skip to question 8. Otherwise, answer part (b).

(b) Does any of the published literature cited reference a specific (e.g. brand name) product? Note that if yes, the applicant will be required to submit patent certification for the product, see question 12.

8. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").

9. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA may refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)). YES NO

10. Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application may be refused for filing under 21 CFR 314.101(d)(9)). YES NO

11. Is the application for a duplicate of a listed drug whose only difference is YES NO

that the rate at which the product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application may be refused for filing under 21 CFR 314.101(d)(9).

12. Are there certifications for each of the patents listed in the Orange Book for the listed drug(s) referenced by the applicant (see question #2)? (This is different from the patent declaration submitted on form FDA 3542 and 3542a.) YES NO

13. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

- Not applicable (e.g., solely based on published literature. See question # 7)
- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)
Patent number(s):

NOTE: IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must **subsequently** submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]. OND will contact you to verify that this documentation was received.

- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).
Patent number(s):
- Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):
- 21 CFR 314.50(i)(1)(ii): No relevant patents.
- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

14. Did the applicant:

- Identify which parts of the application rely on the finding of safety and effectiveness for a listed drug or published literature describing a listed drug or both? For example, pharm/tox section of application relies on finding of preclinical safety for a listed drug.

YES NO

If "Yes," what is the listed drug product(s) and which sections of the 505(b)(2) application rely on the finding of safety and effectiveness or on published literature about that listed drug

Was this listed drug product(s) referenced by the applicant? (see question # 2)

YES NO

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug(s)?

N/A YES NO

15. (a) Is there unexpired exclusivity on this listed drug (for example, 5 year, 3 year, orphan or pediatric exclusivity)? Note: this information is available in the Orange Book.

YES NO

If "Yes," please list:

Application No.	Product No.	Exclusivity Code	Exclusivity Expiration

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/s/

Chantal N. Phillips
1/30/2007 10:56:37 AM
CSO



NDA 22-101

INFORMATION REQUEST LETTER

AstraZeneca LP
Attention: George Kummeth
Global Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Kummeth:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium (esomeprazole) Delayed Released Granules 10 mg.

While reviewing the clinical and labeling portion of your submission, we have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

- 1) For the Study D9614C00097, please submit the following:
 - a) Mean daily exposure to esomeprazole of the safety population (108 patients).
 - b) Duration of the exposure to esomeprazole of the safety population.
- 2) Labeling Comments:

Highlights:

- The Highlights must be limited in length to one-half page, in 8 point type, two-column format. [See 21 CFR 201.57(d)(6) and (d)(8)]
- Add cross references to every statement. The preferred presentation is referencing information corresponding to the location of information in the Full Prescribing Information (FPI). For example, Under Indications and Usage, "Treatment of Gastroesophageal Reflux Disease (GERD) (1.1)."
[See <http://www.fda.gov/cder/regulatory/physLabel/default.htm> for examples of labeling in the new format.]
- List all dosage forms. Add Delayed-Release Granules for Oral Suspension to the drug name that follows the Highlights limitation statement.
[See CFR 201.57 (a)(2)]

- Add a Recent Major Changes section to Highlights to contain any changes made to the following sections during the year before approval of this supplement: Boxed Warning, Indications and Usage, Dosage and Administration, Contraindications, Warnings and Precautions. [See CFR 201.57 (a)(5)]
- The new rule [21 CFR 201.57(a)(6)] requires that if a product is a member of an established pharmacologic class, the following statement must appear under the Indications and Usage heading in the Highlights:

“(Drug/Biologic Product) is a (name of class) indicated for (indication(s)).”

Please propose an established pharmacologic class that is scientifically valid AND clinically meaningful to practitioners or provide rationale why a pharmacologic class should be omitted from the Highlights.

- Delete capsule color and other descriptive attributes under Dosage Forms and Strengths in Highlights. This information belongs in the FPI only in Section 3, Dosage Forms and Strengths, and Section 16, How Supplied/Storage and Handling.
- Regarding Contraindications, “theoretical” adverse reactions must not be listed (i.e., hypersensitivity). If the contraindication is not theoretical, then it must be reworded to explain the type and nature of the adverse reaction. The same applies to the Contraindications section in the FPI. [See 21 CFR 201.57(a)(9) and (c)(5)]
- Under Adverse Reactions, delete the “s” at the end of “nauseas” in the last statement.

FPI: Contents:

- The Contents must be limited in length to one-half page, in 8 point type, two-column format. [See <http://www.fda.gov/cder/regulatory/physLabel/default.htm> for examples of labeling in the new format.]
- Create subsection headings that identify the content. Avoid using the word “General.” See 5.1 Warnings and Precautions. This also applies to the FPI.
- The subsections for **14 CLINICAL STUDIES** are not listed and must be included. [See 21 CFR 201.57 (b)]

14.1 Healing of Erosive Esophagitis

14.2 Symptomatic Gastroesophageal Reflux Disease (GERD)
14.3 Risk Reduction of NSAID-Associated Gastric Ulcer
14.4 Helicobacter pylori (H. pylori) Eradication in Patients with
Duodenal Ulcer Disease

- The required footnote “*Sections or subsections omitted from the full prescribing information are not listed.” should be right justified.
[See <http://www.fda.gov/cder/regulatory/physLabel/default.htm> for examples of labeling in the new format.]

FPI:

- Other than the required bolding [See 21 CFR 201.57(d)(1), (d)(5), and (d)(10), please use bold print sparingly. Use another method for emphasis such as italics or underline.
[See <http://www.fda.gov/cder/regulatory/physLabel/default.htm> for examples of labeling in the new format.]
- The preferred presentation of cross-references in the FPI is the section heading followed by the numerical identifier. For example, [*see Clinical Studies (14) and Dosage and Administration (2)*], not [See **Clinical Studies (14)** and **DOSAGE AND ADMINISTRATION. (2)**]. Because cross-references are embedded in the text in the FPI, the use of italics to achieve emphasis is encouraged. Do not use all capital letters or bold print. Please fix all cross-references throughout the labeling.
[Implementation Guidance]
- Under Adverse Reactions, you refer to adverse reactions as “adverse events.” Please refer to the “Guidance for Industry: Adverse Reactions Sections of Labeling for Human Prescription Drug and Biological Products – Content and Format,” available at <http://www.fda.gov/cder/guidance> and revise your Adverse Reactions section accordingly.
- Move the manufacturer’s information from the end of How Supplied/Storage and Handling to the last page of the labeling after the Patient Counseling Information.
- Delete “ _____ ” at the end of the labeling. The revision date at the end of Highlights replaces this information.

b(4)

If you have any questions call Chantal Phillips, Regulatory Project Manager, at 301-796-2259.

Sincerely,

{See appended electronic signature page}

Brian Strongin, Pharm.D.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Brian Strongin
12/27/2006 08:19:23 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-101

Astra Zeneca LP
Attention: George Kummeth
Global Director
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Kummeth:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium (esomeprazole magnesium) Delayed Release Granules for Oral Suspension, 10mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on November 26, 2006, in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Chantal Phillips, Regulatory Project Manager, at (301) 796-2259.

Sincerely,

{See appended electronic signature page}

Brian Strongin, Pharm. D.
Chief Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Brian Strongin
12/7/2006 09:46:06 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-101

INFORMATION REQUEST LETTER

AstraZeneca LP
Attention: George Kummeth
Global Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Kummeth:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium (esomeprazole) Delayed Released Granules 10 mg.

We are reviewing the Statistical section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

- 1) Although this information is currently available, for ease of review we request that you include the following variables for Study D9614C00097 in a **single merged** data set. Please provide these data in electronic format consistent with the guidance, *Regulatory Submissions in Electronic Format; General Considerations*:

Study number D9614C00097;
Investigator or Center code;
Patient number/name;
Treatment name;
Intent-to-Treat/Safety population (yes or no);
Per-Protocol Patient population (yes or no);
Gender;
Age;
Race;
Height;
Weight;
Physician Assessment score (None, mild, Moderate, or Severe) at Baseline;
Physician Assessment score (None, mild, Moderate, or Severe) at Week 2-Visit;
Physician Assessment score (None, mild, Moderate, or Severe) at Week 4-Visit;
Physician Assessment score (None, mild, Moderate, or Severe) at Week 6-Visit;
Physician Assessment score (None, mild, Moderate, or Severe) at Final-Visit;

Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Heartburn at Baseline;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Acid Regurgitation at Baseline;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Epigastric Pain at Baseline;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Hoarseness at Baseline;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Cough at Baseline;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Gagging at Baseline;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Wheezing at Baseline;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Heartburn at Final-Visit;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Acid Regurgitation at Final-Visit;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Epigastric Pain at Final-Visit;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Hoarseness at Final-Visit;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Cough at Final-Visit;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Gagging at Final-Visit;
Patient Diary Assessment of GERD Symptom Score (0 for None, 1 for Mild, 2 for Moderate, and 3 for Severe) for Wheezing at Final-Visit;
Patient had Erosive Esophagitis (EE) at Baseline (Yes or NO);
Patient had Erosive Esophagitis (EE) Improved after Completion of Esomeprazole Therapy (Yes or NO);
Patient had Erosive Esophagitis (EE) healed after Completion of Esomeprazole Therapy (Yes or NO);

- 2) For the Study D9614C00097, please submit the programs used to perform the statistical efficacy analyses presented in Tables 22, 23, 24, 25, and 26 and Graphs 3, 4, and 5 of section 7.2 entitled "Efficacy Results" on page 76 of the Clinical Study Report.
- 3) To the data set described in section 1) above, please add any additional variables (not listed in the above data set) needed for the above analyses. Please modify the programs to allow input data from the data set described by section 1).

If you have any questions, call Chantal Phillips, Regulatory Project Manager, at 301-796-2259.

Sincerely,

{See appended electronic signature page}

Brian Strongin, Pharm.D.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Brian Strongin
12/4/2006 05:07:39 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-101

AstraZeneca LP
Attention: George Kummeth
Global Director
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Kummeth:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium (esomeprazole magnesium) Delayed Release Granules for Oral Suspension, 10mg.

We are responding to your November 6, 2006 correspondence requesting that we reconsider the Standard (S) review classification of this NDA and grant a Priority (P) review.

We have reviewed the referenced material and maintain our position that NDA 22-101 does not qualify for Priority (P) review for the following reasons:

1. A similar formulation to the NEXIUM granules for oral suspension already exists. Prevacid is a Proton Pump Inhibitor that has already been approved for the treatment of pediatric GERD patients aged 1 to 11 years.
2. With respect to submissions in response to a Written Request:
 - a. Per section 5 of BPCA, any supplement to a 505(b) application proposing a labeling change to reflect the results of pediatric studies conducted under section 505A of the Act will be considered a priority supplement (21 U.S.C. 355a(i)). *The priority review provisions of the BPCA apply only to supplements; they do not apply to a complete new drug application solely because it contains pediatric information.*
 - b. If the supplement proposes a labeling change based on a pediatric study conducted in response to a Written Request, that supplement would receive a priority review, even if the studies submitted did not respond completely to the Written Request and did not otherwise qualify for pediatric exclusivity.

3. Pediatric assessments (studies) conducted outside of a Written Request (i.e., studies conducted and submitted under PREA) are not subject to automatic priority review status. These submissions should be treated like any other submission with respect to a priority review designation.

If you have any questions, call Chantal Phillips, Regulatory Project Manager, at 301-796-2259.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Joyce Korvick
11/21/2006 04:27:29 PM

REQUEST FOR CONSULTATION

(Office/Division): Grace Carmouze, Pediatrics, White Oak, Building #22 Room 6460

FROM (Name, Office/Division, and Phone Number of Requestor):

Chantal Phillips, GI Products, White Oak, Building #22 Room 5121

DATE
November 2, 2006

IND NO.

NDA NO.
22-101

TYPE OF DOCUMENT
New Drug Application

DATE OF DOCUMENT
September 27, 2006

NAME OF DRUG
Nexium

PRIORITY CONSIDERATION
standard

CLASSIFICATION OF DRUG
PPI

DESIRED COMPLETION DATE

NAME OF FIRM: Astra Zeneca

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
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| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: New drug application submitted for a new delayed-release granules for oral suspension formulation of Nexium and revisions to pediatric section of the package insert for patients aged 1-11 yrs. Reference is made to Agency's Written Request for pediatric studies to NDA 21-153. This submission is a partial fulfillment of the Written Request. Please note that this application was submitted electronically and may be found on the EDR pathway-N 22101/27Sept2006. Your input is requested for labeling and the labeling meetings commence on May 16, 2007. Please let me know if you require additional information. Thank you in advance, Chantal Phillips
301-796-2259

SIGNATURE OF REQUESTOR
Chantal Phillips

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Chantal N. Phillips
11/2/2006 02:01:38 PM

REQUEST FOR CONSULTATION

(Office/Division): Michael Brony, DDMAC, White Oak,
Building #22 Room 1469

FROM (Name, Office/Division, and Phone Number of Requestor):
Chantal Phillips, GI Products, White Oak, Building #22
Room 5121

DATE November 1, 2006	IND NO.	NDA NO. 22-101	TYPE OF DOCUMENT New Drug Application	DATE OF DOCUMENT September 27, 2006
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NAME OF DRUG Nexium	PRIORITY CONSIDERATION standard	CLASSIFICATION OF DRUG PPI	DESIRED COMPLETION DATE
------------------------	------------------------------------	-------------------------------	-------------------------

NAME OF FIRM: Astra Zeneca

REASON FOR REQUEST

I. GENERAL

- | | | |
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| <input type="checkbox"/> NEW PROTOCOL
<input type="checkbox"/> PROGRESS REPORT
<input type="checkbox"/> NEW CORRESPONDENCE
<input type="checkbox"/> DRUG ADVERTISING
<input type="checkbox"/> ADVERSE REACTION REPORT
<input type="checkbox"/> MANUFACTURING CHANGE / ADDITION
<input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> PRE-NDA MEETING
<input type="checkbox"/> END-OF-PHASE 2a MEETING
<input type="checkbox"/> END-OF-PHASE 2 MEETING
<input type="checkbox"/> RESUBMISSION
<input type="checkbox"/> SAFETY / EFFICACY
<input type="checkbox"/> PAPER NDA
<input type="checkbox"/> CONTROL SUPPLEMENT | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER
<input type="checkbox"/> FINAL PRINTED LABELING
<input type="checkbox"/> LABELING REVISION
<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE
<input type="checkbox"/> FORMULATIVE REVIEW
<input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
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II. BIOMETRICS

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| <input type="checkbox"/> PRIORITY P NDA REVIEW
<input type="checkbox"/> END-OF-PHASE 2 MEETING
<input type="checkbox"/> CONTROLLED STUDIES
<input type="checkbox"/> PROTOCOL REVIEW
<input type="checkbox"/> OTHER (SPECIFY BELOW): | <input type="checkbox"/> CHEMISTRY REVIEW
<input type="checkbox"/> PHARMACOLOGY
<input type="checkbox"/> BIOPHARMACEUTICS
<input type="checkbox"/> OTHER (SPECIFY BELOW): |
|---|--|

III. BIOPHARMACEUTICS

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| <input type="checkbox"/> DISSOLUTION
<input type="checkbox"/> BIOAVAILABILITY STUDIES
<input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE
<input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS
<input type="checkbox"/> IN-VIVO WAIVER REQUEST |
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IV. DRUG SAFETY

- | | |
|---|---|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
<input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
<input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)
<input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
<input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE
<input type="checkbox"/> POISON RISK ANALYSIS |
|---|---|

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: New drug application submitted for a new delayed-release granules for oral suspension formulation of Nexium and revisions to pediatric section of the package insert for patients aged 1-11 yrs. Please note that this application was submitted electronically and may be found on the EDR pathway-N 22101/27Sept2006/labeling. Please let me know if you require additional information. Thank you in advance, Chantal Phillips 301-796-2259

SIGNATURE OF REQUESTOR
Chantal Phillips

METHOD OF DELIVERY (Check one)
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PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Chantal N. Phillips
11/2/2006 01:42:14 PM

REQUEST FOR CONSULTATION

To (Office/Division): Diane Smith, DMETS, White Oak, Rm 5121

FROM (Name, Office/Division, and Phone Number of Requestor):

Chantal Phillips, GI Products, White Oak, Building #22 Room 5121

DATE November 1, 2006	IND NO.	NDA NO. 22-101	TYPE OF DOCUMENT New Drug Application	DATE OF DOCUMENT September 27, 2006
--------------------------	---------	-------------------	--	--

NAME OF DRUG Nexium	PRIORITY CONSIDERATION standard	CLASSIFICATION OF DRUG PPI	DESIRED COMPLETION DATE
------------------------	------------------------------------	-------------------------------	-------------------------

NAME OF FIRM: Astra Zeneca

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|---|--|
| <input type="checkbox"/> NEW PROTOCOL
<input type="checkbox"/> PROGRESS REPORT
<input type="checkbox"/> NEW CORRESPONDENCE
<input type="checkbox"/> DRUG ADVERTISING
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<input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> PRE-NDA MEETING
<input type="checkbox"/> END-OF-PHASE 2a MEETING
<input type="checkbox"/> END-OF-PHASE 2 MEETING
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<input type="checkbox"/> CONTROL SUPPLEMENT | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER
<input type="checkbox"/> FINAL PRINTED LABELING
<input type="checkbox"/> LABELING REVISION
<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE
<input type="checkbox"/> FORMULATIVE REVIEW
<input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
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II. BIOMETRICS

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<input type="checkbox"/> CONTROLLED STUDIES
<input type="checkbox"/> PROTOCOL REVIEW
<input type="checkbox"/> OTHER (SPECIFY BELOW): | <input type="checkbox"/> CHEMISTRY REVIEW
<input type="checkbox"/> PHARMACOLOGY
<input type="checkbox"/> BIOPHARMACEUTICS
<input type="checkbox"/> OTHER (SPECIFY BELOW): |
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III. BIOPHARMACEUTICS

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| <input type="checkbox"/> DISSOLUTION
<input type="checkbox"/> BIOAVAILABILITY STUDIES
<input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE
<input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS
<input type="checkbox"/> IN-VIVO WAIVER REQUEST |
|--|--|

IV. DRUG SAFETY

- | | |
|---|---|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
<input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
<input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)
<input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
<input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE
<input type="checkbox"/> POISON RISK ANALYSIS |
|---|---|

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: New drug application submitted for a new delayed-release granules for oral suspension formulation of Nexium and revisions to pediatric section of the package insert for patients aged 1-11 yrs. Please note that this application was submitted electronically and may be found on the EDR pathway-N 22101/27Sept2006/labeling. We are asking you to review the package insert because the trade name has already been approved (NDA 21957). Please let me know if you require additional information. Thank you in advance, Chantal Phillips
301-796-2259

SIGNATURE OF REQUESTOR
Chantal Phillips

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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

/s/

Chantal N. Phillips
11/2/2006 01:50:58 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-101

NDA ACKNOWLEDGMENT

Astra Zeneca LP
Attention: George Kummeth
Global Director
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Mr. Kummeth:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	Nexium, (esomeprazole magnesium) Delayed-Release Granules for Oral Suspension, 10mg.
Review Priority Classification:	Standard (S)
Date of Application:	September 27, 2006
Date of Receipt:	September 27, 2006
Our Reference Number:	NDA 22-101

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on November 27, 2006 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be July 27, 2007.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have submitted pediatric studies with this application. Once the review of this application is complete we will notify you whether you have fulfilled the pediatric study requirement for this application.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

NDA 22-101

Page 2

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastroenterology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Chantal Phillips, Regulatory Project Manager, at
(301) 796-2259.

Sincerely,

{See appended electronic signature page}

Chantal Phillips, LCDR
Regulatory Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Chantal N. Phillips
10/13/2006 02:02:13 PM