APPLICATION NUMBER: 21-957

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
**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

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

<table>
<thead>
<tr>
<th>TRADE NAME (OR PROPOSED TRADE NAME)</th>
<th>NEXIUM® Delayed-Release Granules for Oral Suspension</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTIVE INGREDIENT(S)</td>
<td>Esomeprazole magnesium</td>
</tr>
<tr>
<td>STRENGTH(S)</td>
<td>20 and 40 mg of Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)</td>
</tr>
<tr>
<td>DOSAGE FORM</td>
<td>oral</td>
</tr>
</tbody>
</table>

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)(i) 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.

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**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 | 6,875,872 |
| b. Issue Date of Patent | 4/5/2005 |
| c. Expiration Date of Patent | 5/27/2014 |
| d. Name of Patent Owner | AstraZeneca AB |
| Address (of Patent Owner) | SE-151 85 |
| City/State | Sodertalje, Sweden |
| ZIP Code | SE-151 85 |
| FAX Number (If available) | 01146855326000 |
| Telephone Number | 01146855326000 |
| 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 (g)(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) | Vice President, General Counsel & Compliance Officer |
| 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) | AstraZeneca Pharmaceuticals LP |

**C**

| 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)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>* 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.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3 If the answer to question 2.2 is &quot;Yes,&quot; 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).</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2.6 Does the patent claim only an intermediate?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>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.)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

### 3. Drug Product (Composition/Formulation)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.2 Does the patent claim only an intermediate?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>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.)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

### 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:

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2 Patent Claim Number (as listed in the patent) 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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2a If the answer to 4.2 is &quot;Yes,&quot; 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.)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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

6.1 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.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

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

[Signature]

Date Signed: 11/5/05

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, General Counsel & Compliance Officer

Address: 1800 Concord Pike
City/State: Wilmington, DE

ZIP Code: 19803
Telephone Number: (302) 886-3000

FAX Number (if available): 302-886-1378
E-Mail Address (if available): Glenn.Englemann@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-407)
5000 Fisher's 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.
INFORMATION AND INSTRUCTIONS FOR FORM 3542a

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

• To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.

• Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.

• Form 3542 should be used when submitting patent information relating to an approved supplement under 21 CFR 314.53(e) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.

• Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."

• Only information from form 3542 will be used for Orange Book Publication purposes.

• Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.

• The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.

• Additional copies of these forms may be downloaded from the Internet at: http://forms.fda.gov/forms/fda3542a.html.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2a) Name the polymorphic form of the drug identified by the patent.

2b) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2c) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3a) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6a) Authorized signature. Check one of the four boxes that best describes the authorized signature.
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 Granules for Oral Suspension

**ACTIVE INGREDIENT(S)**
Esomeprazole magnesium

**STRENGTH(S)**
20 mg and 40 mg Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)

**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.

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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
      6,428,810
   b. Issue Date of Patent
      8/6/2002
   c. Expiration Date of Patent
      11/3/2019
   d. Name of Patent Owner
      AstraZeneca AB
      Address (of Patent Owner)
      SE-151 85
      City/State
      Södertälje, Sweden
      ZIP Code
      SE-151 85
      FAX Number (if available)
      Telephone Number
      01146855326000
      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)
      Vice President, General Counsel & Compliance Officer
      AstraZeneca Pharmaceuticals LP
      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)
   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

FORM FDA 3542a (7/03)
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?  

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?  

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).  

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

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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.)

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?  

3.2 Does the patent claim only an intermediate?

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.)

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?  

4.2 Patent Claim Number (as listed in the patent)  

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 Granules Label at DESCRIPTION, 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.
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Check applicable box and provide information below.

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

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

Name
Glenn M Engelman, Vice President, General Counsel & Compliance Officer

Address
1800 Concord Pike
City/State
Wilmington, DE

ZIP Code
19803
Telephone Number
(302) 886-3244

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-300)
3600 Fisher's 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.
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First Section
Complete all items in this section.

1. General Section

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4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4d) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.
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**1. GENERAL**

<table>
<thead>
<tr>
<th>a. United States Patent Number</th>
<th>6,369,085</th>
</tr>
</thead>
<tbody>
<tr>
<td>c.Expiration Date of Patent</td>
<td>5/25/2018</td>
</tr>
<tr>
<td>d. Name of Patent Owner</td>
<td>AstraZeneca AB</td>
</tr>
<tr>
<td>Address (of Patent Owner)</td>
<td>SE-151 85</td>
</tr>
<tr>
<td>City/State</td>
<td>Södertälje, Sweden</td>
</tr>
<tr>
<td>ZIP Code</td>
<td>SE-151 85</td>
</tr>
<tr>
<td>FAX Number (if available)</td>
<td></td>
</tr>
<tr>
<td>Telephone Number</td>
<td>01146855326000</td>
</tr>
<tr>
<td>E-Mail Address (if available)</td>
<td></td>
</tr>
<tr>
<td>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 (b)(3)(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)</td>
<td>Vice President, General Counsel &amp; Compliance Officer AstraZeneca Pharmaceuticals LP</td>
</tr>
<tr>
<td>Address (of agent or representative named in 1.e.)</td>
<td>1800 Concord Pike</td>
</tr>
<tr>
<td>City/State</td>
<td>Wilmington, DE</td>
</tr>
<tr>
<td>ZIP Code</td>
<td>19803</td>
</tr>
<tr>
<td>FAX Number (if available)</td>
<td></td>
</tr>
<tr>
<td>Telephone Number</td>
<td>(800) 456-3669</td>
</tr>
<tr>
<td>E-Mail Address (if available)</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
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</table>

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

<table>
<thead>
<tr>
<th>Yes</th>
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</table>
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)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
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<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>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.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>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(h).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.6 Does the patent claim only an intermediate?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.)</td>
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<td></td>
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</table>

### 3. Drug Product (Composition/Formulation)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.2 Does the patent claim only an intermediate?</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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:

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2 Patent Claim Number (as listed in the patent) 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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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 Granules in Label at DESCRIPTION, INDICATIONS AND USAGE. Information for Patients DOSAGE AND ADMINISTRATION.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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

6.1 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.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

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

[Signature]

Date Signed 11/6/05

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

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

Name Glenn M Engelman, Vice President, General Counsel & Compliance Officer

Address 1800 Concord Pike

City/State Wilmington, DE

ZIP Code 19803

Telephone Number (302) 886-3244

FAX Number (if available) (302) 886-1578

E-Mail Address (if available) glenn.engelman@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.
INFORMATION AND INSTRUCTIONS FOR FORM 3542a
PATENT INFORMATION SUBMITTED WITH THE FILING
OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions. NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book Publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: http://forms.fda.gov/forms/fdAlright/fdAlright.html.

First Section
Complete all items in this section.

1. General Section
Complete all items in this section with reference to the patent itself.

1c) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)
Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)
Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use
Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents
Complete this section only if applicable.

6. Declaration Certification
Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.
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 Granules for Oral Suspension

ACTIVE INGREDIENT(S)
Esomeprazole magnesium

STRENGTH(S)
20 mg and 40 mg Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)

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 handwritten 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
5,900,424

b. Issue Date of Patent
5/4/1999

c. Expiration Date of Patent
5/4/2016

d. Name of Patent Owner
AstraZeneca AB

Address (of Patent Owner)
SE-151 85

City/State
Södertälje, Sweden

ZIP Code
SE-151 85

Telephone Number
01146855326000

E-Mail Address (if available)

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)

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</tr>
<tr>
<td>2.3 If the answer to question 2.2 is &quot;Yes,&quot; 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).</td>
<td>☒</td>
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### 3. Drug Product (Composition/Formulation)

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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:

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<td>☐</td>
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<tr>
<td>4.2 Patent Claim Number (as listed in the patent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2a 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?</td>
<td>☒</td>
<td>☐</td>
</tr>
<tr>
<td>4.2a If the answer to 4.2 is &quot;Yes,&quot; 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.)</td>
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<td></td>
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<tr>
<td>4.2a</td>
<td>See NEXIUM Delayed Release Granules in Label at DESCRIPTION, INDICATIONS AND USAGE. Information for Patients DOSAGE AND ADMINISTRATION.</td>
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### 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

6.1 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.

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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 the FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

- [ ] NDA Applicant/Holder
- [x] NDA Applicant/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, General Counsel & Compliance Officer

Address
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code
19803

Telephone Number
(302) 886-3244

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)
3500 Fisher's 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.
INFORMATION AND INSTRUCTIONS FOR FORM 3542a

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

• To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.

• Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.

• Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.

• Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."

• Only information from form 3542 will be used for Orange Book Publication purposes.

• Forms should be submitted as described in 21 CFR 314.33. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.

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First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

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2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.
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 Granules for Oral Suspension

**ACTIVE INGREDIENT(S)**

Esomeprazole magnesium

**STRENGTH(S)**

20 mg and 40 mg Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)

**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

5,877,192

b. Issue Date of Patent

3/2/1999

c. Expiration Date of Patent

5/27/2014

d. Name of Patent Owner

AstraZeneca AB

Address (of Patent Owner)

SE-151 85

City/State

Södertälje, Sweden

ZIP Code

SE-151 85

FAX Number (if available)

01146855326000

Telephone Number

E-Mail Address (if available)

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

☐ Yes  ☐ No

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☐ Yes  ☐ No

---

**FORM FDA 3542a (7/03)**

Page 1
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<td>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.)</td>
<td>□ Yes □ No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Method of Use</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>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:</td>
<td></td>
</tr>
<tr>
<td>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?</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>4.2 Patent Claim Number (as listed in the patent)</td>
<td>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?</td>
</tr>
<tr>
<td>1, 2, 5, 6, 10, 11 and 23</td>
<td></td>
</tr>
<tr>
<td>4.2a If the answer to 4.2 is &quot;Yes,&quot; identify with specificity the use with reference to the proposed labeling for the drug product.</td>
<td>Use: (Submit indication or method of use information as identified specifically in the approved labeling.) See NEXIUM Delayed Release Granules in Label at DESCRIPTION, INDICATIONS AND USAGE, Information for Patients DOSAGE AND ADMINISTRATION.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. No Relevant Patents</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>□ Yes</td>
</tr>
</tbody>
</table>

| 6. Declaration Certification |  |
6.1 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.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

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

|☐ NDA Applicant/Holder | ☒ NDA Applicant/Holder's Attorney, Agent (Representative) or other Authorized Official |
|☐ Patent Owner | ☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official |

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.

Name
Glenn M Engelmann, Vice President, General Counsel & Compliance Officer

Address
1800 Concord Pike

ZIP Code
19803

Telephone Number
(302) 886-3244

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-807)
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.
INFORMATION AND INSTRUCTIONS FOR FORM 3542a
PATENT INFORMATION SUBMITTED WITH THE FILING
OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.

Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.

Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.

Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."

Only information from form 3542 will be used for Orange Book Publication purposes.

Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.

The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.

Additional copies of these forms may be downloaded from the Internet at: http://forms.psc.gov/forms/fdahtm/fdahtm.html.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.
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

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 Granule for Oral Suspension

ACTIVE INGREDIENT(S)          STRENGTH(S)
Esomeprazole magnesium         20 mg and 40 mg Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)

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
   5,714,504

b. Issue Date of Patent
   2/3/1998

c. Expiration Date of Patent
   2/3/2015

d. Name of Patent Owner
   AstraZeneca AB

Address (of Patent Owner)
SE-151 85
City/State
Södertälje, Sweden
ZIP Code
SE-151 85
FAX Number (if available)
Telephone Number
01146855326000
E-Mail Address (if available)

f. 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 sections 505(b)(3) and (g)(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)

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)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3 If the answer to question 2.2 is &quot;Yes,&quot; 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).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.6 Does the patent claim only an intermediate?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 3. Drug Product (Composition/Formulation)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.2 Does the patent claim only an intermediate?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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:

<table>
<thead>
<tr>
<th>Patent Claim Number (as listed in the patent)</th>
<th>6, 7, 10</th>
<th>Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.2a If the answer to 4.2 is &quot;Yes,&quot; identify with specificity the use with reference to the proposed labeling for the drug product.</td>
<td>Use: (Submit indication or method of use information as identified specifically in the approved labeling.) See NEXIUM Delayed Release Granules in Label at DESCRIPTION, INDICATIONS AND USAGE. Information for Patients DOSAGE AND ADMINISTRATION.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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

FORM FDA 3542a (7/03)
6.1 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.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

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

<table>
<thead>
<tr>
<th>NDA Applicant/Holder</th>
<th>NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>☒</td>
</tr>
</tbody>
</table>

Date Signed: 11/8/05

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.

<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
<th>City/State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glenn M Engelmann, Vice President, General Counsel &amp; Compliance Officer</td>
<td>1500 Concord Pike</td>
<td>Wilmington, DE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ZIP Code</th>
<th>Telephone Number</th>
<th>E-Mail Address (if available)</th>
</tr>
</thead>
<tbody>
<tr>
<td>19803</td>
<td>(302) 886-3244</td>
<td><a href="mailto:glenn.engelmann@astrazeneca.com">glenn.engelmann@astrazeneca.com</a></td>
</tr>
</tbody>
</table>

FAX Number (if available): (302) 886-1578

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-507)
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.
INFORMATION AND INSTRUCTIONS FOR FORM 3542a

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

• To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.

• Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.

• Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.

• Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."

• Only information from form 3542 will be used for Orange Book Publication purposes.

• Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.

• The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.

• Additional copies of these forms may be downloaded from the Internet at: http://forms.fda.gov/forms/fdalint/fdalint.html.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.
**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

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

<table>
<thead>
<tr>
<th>TRADE NAME (OR PROPOSED TRADE NAME)</th>
<th>NEXIUM® (esomeprazole magnesium) Delayed-Release Granules for Oral Suspension</th>
</tr>
</thead>
</table>

**ACTIVE INGREDIENT(S)**

Esomeprazole magnesium

**STRENGTH(S)**

20 mg and 40 mg Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)

**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(e)(2)(6) 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 sections and sections 5 and 6.

### 1. GENERAL

<table>
<thead>
<tr>
<th>a. United States Patent Number</th>
<th>5,690,960</th>
</tr>
</thead>
<tbody>
<tr>
<td>c. Expiration Date of Patent</td>
<td>11/25/2014</td>
</tr>
<tr>
<td>d. Name of Patent Owner</td>
<td>AstraZeneca AB</td>
</tr>
<tr>
<td>Address (of Patent Owner)</td>
<td>SE-151 85</td>
</tr>
<tr>
<td>City/State</td>
<td>Södertälje, Sweden</td>
</tr>
<tr>
<td>ZIP Code</td>
<td>SE-151 85</td>
</tr>
<tr>
<td>FAX Number (if available)</td>
<td></td>
</tr>
<tr>
<td>Telephone Number</td>
<td>01146855326000</td>
</tr>
<tr>
<td>E-Mail Address (if available)</td>
<td></td>
</tr>
<tr>
<td>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)</td>
<td>Vice President, General Counsel &amp; Compliance Officer AstraZeneca Pharmaceuticals LP</td>
</tr>
<tr>
<td>Address (of agent or representative named in e.)</td>
<td>1800 Concord Pike</td>
</tr>
<tr>
<td>City/State</td>
<td>Wilmington, DE</td>
</tr>
<tr>
<td>ZIP Code</td>
<td>19803</td>
</tr>
<tr>
<td>FAX Number (if available)</td>
<td></td>
</tr>
<tr>
<td>Telephone Number</td>
<td>(800) 456-3669</td>
</tr>
<tr>
<td>E-Mail Address (if available)</td>
<td></td>
</tr>
</tbody>
</table>

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

FORM FDA 3542a (7/03)
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 |
| 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) | 17, 18 |
| 4.2a | Does the patent claim referenced in 4.2 claiming a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? | ☑ Yes ☐ No |

**4.2a Use:** (Submit indication or method of use information as identified specifically in the approved labeling.)

See NEXIUM Delayed Release Granules in Label at DESCRIPTION, 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
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.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

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

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/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, General Counsel & Compliance Officer

Address
1800 Concord Pike
City/State
Wilmington, DE

ZIP Code
19803
Telephone Number
(302) 886-3244

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.
INFORMATION AND INSTRUCTIONS FOR FORM 3542a

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book Publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: http://forms.fdas.gov/forms/fdalum/fdalum.html.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1a) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

1b) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

1c) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.
**Trade Name (Or Proposed Trade Name)**
NEXIUM® Delayed-Release Granules for Oral Suspension

**Active Ingredient(s)**
Esomeprazole magnesium

**Strength(s)**
20 and 40 mg of Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)

**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 | 4/19/2006 |

| d. Name of Patent Owner | AB Hässle |
| 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) | Vice President, General Counsel & Compliance Officer 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?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
<td></td>
</tr>
</tbody>
</table>

#### 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?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>❌</td>
</tr>
</tbody>
</table>

* 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).

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>❌</td>
</tr>
</tbody>
</table>

#### 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.)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
<td></td>
</tr>
</tbody>
</table>

#### 2.6 Does the patent claim only an intermediate?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
<td></td>
</tr>
</tbody>
</table>

#### 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.)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
<td></td>
</tr>
</tbody>
</table>

### 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?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
<td></td>
</tr>
</tbody>
</table>

#### 3.2 Does the patent claim only an intermediate?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
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</tr>
</tbody>
</table>

#### 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.)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
<td></td>
</tr>
</tbody>
</table>

### 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?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
<td></td>
</tr>
</tbody>
</table>

#### 4.2 Patent Claim Number (as listed in the patent)

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>❌</td>
<td></td>
</tr>
</tbody>
</table>

**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 NEXUM Delayed Release Granules in Label at DESCRIPTION, 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.

<table>
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<th>Yes</th>
<th>No</th>
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<td></td>
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6. Declaration Certification

6.1 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.

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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 Engelman, Vice President, General Counsel & Compliance Officer

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.engelman@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

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INFORMATION AND INSTRUCTIONS FOR FORM 3542a
PATENT INFORMATION SUBMITTED WITH THE FILING
OF AN NDA, AMENDMENT OR SUPPLEMENT

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- To submit patent information to the agency, the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.

- Form 3542a should be used when submitting patent information with original NDA submissions. NDA amendments and NDA supplements prior to approval.

- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.

- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."

- Only information from form 3542 will be used for Orange Book Publication purposes.

- Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.

- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.

- Additional copies of these forms may be downloaded from the Internet at: http://forms.fda.gov/forms/idatime/idatime.html.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1.1) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

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2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

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2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.
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 Granules for Oral Suspension

ACTIVE INGREDIENT(S)
Esomeprazole magnesium

STRENGTH(S)
20 mg and 40 mg Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)

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
4,786,505

b. Issue Date of Patent
11/22/1988

c. Expiration Date of Patent
4/20/2007

d. Name of Patent Owner
AB Hässle

Address (of Patent Owner)
SE-431 83

City/State
Mölndal, Sweden

ZIP Code
SE-431 83

FAX Number (if available)

Telephone Number
01146317761000

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 (g)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.96 (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 a.):
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code
19803

FAX Number (if available)

Telephone Number
(800) 456-3669

E-Mail Address (if available)

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)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3 If the answer to question 2.2 is &quot;Yes,&quot; 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).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.6 Does the patent claim only an intermediate?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 3. Drug Product (Composition/Formulation)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.2 Does the patent claim only an intermediate?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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:

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2 Patent Claim Number (as listed in the patent) 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?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2a If the answer to 4.2 is &quot;Yes,&quot; 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 Granules in Label at DESCRIPTION, INDICATIONS AND USAGE, Information for Patients DOSAGE AND ADMINISTRATION</td>
<td></td>
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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.

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Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

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

Date Signed

11/8/05

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(o)(4) and (d)(4).

Check applicable box and provide information below.

☐ NDA Applicant/Holder

☐ Patent Owner

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

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

Name
Glenn M Engelmann, Vice President, General Counsel & Compliance Officer

Address
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code
19803

Telephone Number
(302) 886-3244

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 (HF-2407)
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.
INFORMATION AND INSTRUCTIONS FOR FORM 3542a
PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

• To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.

• Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments, and NDA supplements prior to approval.

• Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.

• Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."

• Only information from form 3542 will be used for Orange Book Publication purposes.

• Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.

• The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.

• Additional copies of these forms may be downloaded from the Internet at: http://forms.psc.gov/forms/fdahm/fdahm.html.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.
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 Granules for Oral Suspension

**ACTIVE INGREDIENT(S)**

Esomeprazole magnesium

**STRENGTH(S)**

- 20 mg and 40 mg Esomeprazole (22.3 mg and 44.5 mg esomeprazole magnesium trihydrate)

**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

| b. Issue Date of Patent | 8/1/1989 |
| c. Expiration Date of Patent | 4/20/2007 |
| d. Name of Patent Owner | AB Håssle |
| Address of Patent Owner | SE-43183 |
| City/State | Mölndal, Sweden |
| ZIP Code | SE-43183 |
| Telephone Number | 01146317761000 |
| 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)**

Vice President, General Counsel & Compliance Officer
AstraZeneca Pharmaceuticals LP

Address of agent or representative named in note)
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code | 19803 |
| Telephone Number | (800) 456-3669 |
| E-Mail Address (if available) | |

### 2. PATENT

| United States Patent Number | 4,853,230 |
| Issue Date of Patent | 8/1/1989 |
| Expiration Date of Patent | 4/20/2007 |
| Name of Patent Owner | AB Håssle |
| Address of Patent Owner | SE-43183 |
| City/State | Mölndal, Sweden |
| ZIP Code | SE-43183 |
| Telephone Number | 01146317761000 |
| E-Mail Address (if available) | |

**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

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)  
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 Granules in Label at DESCRIPTION, 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
6.1 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.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

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

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, General Counsel & Compliance Officer

Address
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code
19803

Telephone Number
(302) 886-3244

FAX Number (if available)
(302) 886-1578

E-Mail Address (if available)
glenn.engelmann@astrazeneca.com

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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 # 21-957 SUPPL # HFD # 180

Trade Name NEXIUM

Generic Name esomeprazole magnesium for Delayed Release Oral Suspension

Applicant Name AstraZeneca

Approval Date, If Known 10/22/06

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.

   Study compares bioequivalence of NEXIUM capsules (NDA 21-153) and the proposed NEXIUM for oral suspension (NDA 21-957)

   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?

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?

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 #(#).
NDA# 21-153  NEXIUM (esomeprazole magnesium) For Delayed Release Capsules

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:

Sponsor conducted bioequivalency studies to show Bioequivalency to the approved capsule formulation (NDA 21-153).

(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?
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:

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.")

<table>
<thead>
<tr>
<th>Investigation #1</th>
<th>YES □</th>
<th>NO □</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigation #2</td>
<td>YES □</td>
<td>NO □</td>
</tr>
</tbody>
</table>

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?

<table>
<thead>
<tr>
<th>Investigation #1</th>
<th>YES □</th>
<th>NO □</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigation #2</td>
<td>YES □</td>
<td>NO □</td>
</tr>
</tbody>
</table>
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"): 

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?

<table>
<thead>
<tr>
<th>Investigation #1</th>
<th>IND #</th>
<th>YES □</th>
<th>NO □</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>!</td>
<td>!</td>
</tr>
</tbody>
</table>

Explain:

Investigation #2

<table>
<thead>
<tr>
<th>Investigation #2</th>
<th>IND #</th>
<th>YES □</th>
<th>NO □</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>!</td>
<td>!</td>
</tr>
</tbody>
</table>

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 □ NO □
Explain: Explain:

Investigation #2

YES □ NO □
Explain: 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: Marlene G. Swider
Title: Regulatory Project Manager
Date: 10/19/06

Name of Office/Division Director signing form: Joyce A. Korvick, M.D., M.P.H.
Title: Deputy Director, Division of Gastroenterology Products

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/

Brian Harvey
10/23/2006 05:03:54 PM
For Dr. Joyce Korvick
NDA/BLA #: 21-957
Supplement Type (e.g. SE5): SE
Supplement Number:

Stamp Date: 12/22/05
PDUSA Goal Date: 10/22/06

HFD 180 Trade and generic names/dosage form: esomeprazole magnesium/oral suspension

Applicant: AstraZeneca
Therapeutic Class: Proton Pump Inhibitor (PPI)

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 section.
☐ 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 Carmine.

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): 4


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 (Birth - 11 yrs) X Completed (Ages 12 - 17)

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. Enter into RMS/BLA Communication as Memo/Other (OT) - Summary Text: Pediatric Page and update the special characteristics code in RMS/BLA with Fed Studies Waived.
Section B: Partially Waived Studies

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

<table>
<thead>
<tr>
<th>Min</th>
<th>kg</th>
<th>mo.</th>
<th>yr.</th>
<th>Tanner Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max</td>
<td>kg</td>
<td>mo.</td>
<td>yr.</td>
<td>Tanner Stage</td>
</tr>
</tbody>
</table>

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 RMS-BLA. Enter into CBER Communication as: Memo/Other (OT) - Summary Text: Pediatric Page, and update the special characteristics code in RMS/BLA with Ped Studies Partially Waived.

Section C: Deferred Studies

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

<table>
<thead>
<tr>
<th>Min</th>
<th>kg</th>
<th>mo.</th>
<th>yr.</th>
<th>Tanner Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max</td>
<td>kg</td>
<td>mo.</td>
<td>yr.</td>
<td>Tanner Stage</td>
</tr>
</tbody>
</table>

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: ________________________________

Date studies are due (mm/dd/yy): ________________

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into RMS-BLA. Enter into CBER Communication as: Memo/Other (OT) - Summary Text: Pediatric Page, and update the special characteristics code in RMS/BLA with Ped Studies Deferred.

Section D: Completed Studies

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

<table>
<thead>
<tr>
<th>Min</th>
<th>kg</th>
<th>mo.</th>
<th>yr.</th>
<th>Tanner Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max</td>
<td>kg</td>
<td>mo.</td>
<td>yr.</td>
<td>Tanner Stage</td>
</tr>
</tbody>
</table>

Comments: As the date of approval for this NDA, only studies for ages 12-17 have been approved. Results for studies for ages 1-11 are still being reviewed by FDA.

Comments: As the date of approval for this NDA, only studies for ages 12-17 have been approved. Results for studies for ages 1-11 are still being reviewed by FDA.
If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into RMS-BLA. Enter into CBER Communication as Memo/Other (OT) - Summary Text: Pediatric Page, and update the special characteristics code in RMS-BLA with Fed Data Submitted and Complete.

This page was completed by:

[See appended electronic signature page]

Regulatory Project Manager

cc: NDA 21-957
Rosemary Addy or Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT ROSEMARY ADDY OR GRACE CARMOUZE

(revised for TBP licensing products 9-15-2006)
Attachment A

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

Indication #2: Risk Reduction of NSAID - Associated Gastric Ulcer

Is this an orphan indication?

☐ Yes: PMEA 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. Enter into RMS-BLA Communication as Memo/Other (OT), Summary Text: Pediatric Page, and update the special characteristics code in RMS/BLA with Fed Studies Waived.

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 RMS-BLA. Enter into OBER Communication as Memo/Other (OT), Summary Text: Pediatric Page, and update the special characteristics code in RMS/BLA with Fed Studies Partially Waived.
Section C: Deferred Studies

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

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

Reason(s) for deferral:

☐ Products in this class for this indication have been studied/labelled 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:

Date studies are due (mm/dd/yy): __________________________

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into RMS:BLA. Enter into CBER Communication as: Memo/Other OT - SummaryText, Pediatric Page, and update the special characteristics code in RMS:BLA with Ped Studies Deferred.

Section D: Completed Studies

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

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

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into RMS:BLA. Enter into CBER Communication as: Memo/Other OT - SummaryText, Pediatric Page, and update the special characteristics code in RMS:BLA with Ped Date Submitted and Complete.

This page was completed by:

[See appended electronic signature page]

[Signature]

Regulatory Project Manager

cc:  NDA 21-957
Rosemary Addy or Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT ROSEMARY ADDY OR GRACE CARMOUZE

(revised for TBP licensing products 9-15-2006)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)
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. Enter into RMS-BLA Communication as Memo/Other (O) - Summary Text: Pediatric Page and update the special characteristics code in RMS-BLA with Ped Studies Waived.

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 RMS-BLA. Enter into CIR/R Communication as: Memo/Other (O) - Summary Text: Pediatric Page and update the special characteristics code in RMS-BLA with Ped Studies Partially Waived.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):
Section D: Completed Studies

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

<table>
<thead>
<tr>
<th>Min</th>
<th>kg</th>
<th>mo.</th>
<th>yr.</th>
<th>Tanner Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max</td>
<td>kg</td>
<td>mo.</td>
<td>yr.</td>
<td>Tanner Stage</td>
</tr>
</tbody>
</table>

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into RMS/BLA. Enter into CBER Communication as: Memo/Other (OT) - SummaryText: Pediatric Page; and update the special characteristics code in RMS/BLA with Ped Studies Defered.

This page was completed by:

[See appended electronic signature page]

Regulatory Project Manager

cc: NDA 21-957
Rosemary Addy or Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT ROSEMARY ADDY OR GRACE CARMOUZE

(revised for TBP licensing products 9-15-2006)

Attachment A

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

Indication #4: Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome

Is this an orphan indication?

☐ Yes: PREA does not apply. Skip to signature block.
Is there a full waiver for this indication (check one)?

☐ No: Please proceed to the next question.

☒ 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. Enter into RMS-BLA Communication as: Memo/Other (OT) - Summary Text - Pediatric Page; and update the special characteristics code in RMS/BLA with Ped Studies Waived.

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 RMS-BLA. Enter into CBER Communication as: Memo/Other (OT) - Summary Text - Pediatric Page; and update the special characteristics code in RMS/BLA with Ped Studies Partially Waived.

Section C: Deferred Studies

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

Min  kg  mo.  yr.  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
NDA 21-957
Page 9

☐ 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: ____________________________

Date studies are due (mm/dd/yy): __________

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into RMS-BLA. Enter into CBER Communication as: Memo/Other (OT) - SummaryText: Pediatric Page; and update the special characteristics code in RMS/BLA with Ped Studies Deferred.

Section D: Completed Studies

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

Min. ___________ kg ___________ no. __________ yr. __________ Tanner Stage __________
Max. ___________ kg ___________ no. __________ yr. __________ Tanner Stage __________

Comments: ____________________________________________________________

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into RMS-BLA. Enter into CBER Communication as: Memo/Other (OT) - SummaryText: Pediatric Page; and update the special characteristics code in RMS/BLA with Ped Data Submitted and Complete.

This page was completed by:

(See appended electronic signature page)

Regulatory Project Manager

cc: NDA 21-957
Rosemary Addy or Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT ROSEMARY ADDY OR GRACE CARMOUZE

(revised for TBP licensing products 9-15-2006)
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Joyce Korvick
10/20/2006 02:13:40 PM
ITEM 16  DEBARMENT CERTIFICATION

Re:  NDA 21-957

NEXIUM® (esomeprazole magnesium) Delayed-Release 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 21-957 (Study Number D9612C00032) the services of any person in any capacity debarred under section 306 (a) or (b).

Sincerely,

Anthony Rogers, Vice President
Regulatory Affairs
AstraZeneca
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) Delayed-Release Oral Suspension

Review Priority Classification:  Standard (S)

Date of Application:  December 22, 2005

Date of Receipt:  December 22, 2005

Our Reference Number:  NDA 21-957

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 February 20, 2006 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 22, 2006.

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 not fulfilled the requirement. We are deferring submission of your pediatric studies until INSERT DATE. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of section 2 of the Pediatric Research Equity Act (PREA) within 60 days from the
date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. Please note that satisfaction of the requirements in section 2 of PREA alone may not qualify you for pediatric exclusivity.

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:

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 Melissa Hancock Furness, Regulatory Project Manager, at (301) 796-0893.

Sincerely,

(See appended electronic signature page)

Melissa Hancock Furness
Regulatory Health Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Melissa Furness
3/16/2006 04:40:01 PM
MEMORANDUM OF TELECON

DATE: August 17, 2006
TIME: 11:00 am

APPLICATION NUMBER: NDA 21-957
PRODUCT: NEXIUM DELAYED-RELEASE GRANULES FOR ORAL

PROPOSED INDICATION: Acute healing and maintenance of erosive esophagitis, and symptomatic gastroesophageal reflux disease risk reduction of NSAID-associated gastric ulcer

BETWEEN:

Name: George A. Kummeth, Director, Regulatory Affairs
Lora Radzieta, Associate Director, Regulatory affairs CMC
Karin Malmqvist-Granlund, Analytical and Pharmaceutical Development
Gunilla I Pettersson, Analytical and Pharmaceutical Development
Eva Blychert, Pharmaceutical Project Manager
Mersedeh Miraliakbari, Associate Director, Regulatory Affairs

Representing: AstraZeneca (AZ)

AND

Name: Marie Kowblansky, Ph.D., Pharmaceutical Assessment Leader,
ONDQA, Division II, Branch III
Milton Sloan, CMC, Ph.D., Chemistry Reviewer
Linda Athey, CMC Project Manager
Giuseppe Randazzo, Project Manager

Representing: Division of Gastroenterology Products, HFD-180 and Office of New Drug Quality Assessment

SUBJECT: Response to our June 23, 2006 CMC information request (IR) letter

Background:
On June 23, 2006 an IR letter was sent to the sponsor listing 4 deficiencies and 3 comments. The primary CMC reviewer Dr. Milton Sloan requested a Tcon to clarify the sponsor’s July 13, 2006 response.
TCon dialogue:

FDA: We reviewed your July 13, 2006 response and recommend you amend your application with one of the following courses of action:

1. Develop alternate tests for acid stage dissolution testing of the product
2. Revise the buffer stage dissolution specification to \% or greater dissolved at 30 minutes

AZ: We understand completely and feel this is a fair recommendation. We need to discuss this internally and will forward a response to the agency.

AZ: Are their any other issues from a CMC perspective?

FDA: CMC stability data and labeling still need to be reviewed.

Giuseppe Randazzo  
Regulatory Project Manager  
Division of Gastroenterology Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Marie Kowblansky, Ph.D.  
Pharmaceutical Assessment Lead  
ONDQA, Division II, Branch III
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Giuseppe Randazzo
8/21/2006 08:36:54 AM
CSO

Marie Kowblansky
8/22/2006 11:27:09 AM
CHEMIST
NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA #  21-957  Supplement #   Efficacy Supplement Type  SE-

Date Filing Review Completed: 2/13/06

Trade Name:  Nexium for Delayed Release Oral Suspension
Established Name:  esomeprazole magnesium
Strengths:  20 and 40 mgs

Applicant:  Astra Zeneca
Agent for Applicant:  N/A

Date of Application:  12/22/05
Date of Receipt:  12/22/05
Date clock started after UN:  N/A
Date of Filing Meeting:  2/13/06
Filing Date:  2/20/06
Action Goal Date (optional):  
User Fee Goal Date:  10/22/06

Indication(s) requested:  Zollinger Ellison Syndrome

Type of Original NDA:  (b)(1)  X  (b)(2)  □

Type of Supplement:  (b)(1)  X  (b)(2)  □

NOTE:
(3) 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 (b)(2) regardless of whether the original NDA was a (b)(1) or (b)(2). If the application is a (b)(2), complete Appendix B.

(4) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or (b)(2) application:
   X  NDA is a (b)(1) application  OR  □  NDA is a (b)(2) application

Therapeutic Classification:  S  X  P
Resubmission after withdrawal?  N/A  Resubmission after refuse to file?  N/A
Chemical Classification:  (1,2,3 etc.)  3
Other (orphan, OTC, etc.):  N/A

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

User Fee Status:  Paid  X  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. 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

Version:  12/15/2004

This is a locked document. If you need to add a comment where there is no field to do so, unlock the document using the following procedure. Click the 'View' tab; drag the cursor down to 'Toolbars'; click on 'Forms.' On the forms toolbar, click the lock/unlock icon (looks like a padlock). This will allow you to insert text outside the provided fields. The form must then be relocked to permit tabbing through the fields.
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 an approved (b)(1) or (b)(2) application? YES X NO □
  If yes, explain: for the NDA 21-153 (capsule formulation)

- Does another drug have orphan drug exclusivity for the same indication? YES □ NO X

- 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 X
  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 X
  If yes, explain:

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

- Does the submission contain an accurate comprehensive index? YES X NO □

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

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

- If an electronic NDA, does it follow the Guidance? N/A □ YES X NO □
  If an electronic NDA, all forms and certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A □ YES X NO □

- Is it an electronic CTD (eCTD)? N/A □ YES X NO □
  If an electronic CTD, 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 X 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 X 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 . . . .”

- Financial Disclosure forms included with authorized signature? **YES** **X** **NO** □
  (Forms 3454 and 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)? **Y** □ **NO** □

- PDUFA and Action Goal dates correct in COMIS? **YES** **X** **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: 53,733

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

- Pre-NDA Meeting(s)? Date(s) ____________________________ NO **X**
  If yes, distribute minutes before filing meeting.

**Project Management**

- Was electronic “Content of Labeling” submitted? **YES** **X** **NO** □
  If no, request in 74-day letter.

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? **YES** **X** **NO** □

- Risk Management Plan consulted to ODS/IO? N/A **X** **YES** □ **NO** □

- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? N/A **X** **NO** □

- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A **X** **YES** □ **NO** □

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A **X** **YES** □ **NO** □

**If Rx-to-OTC Switch application: N/A**

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A □ **YES** □ **NO** □

- Has DOTCDP been notified of the OTC switch application? **YES** □ **NO** □
Clinical: N/A

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

Chemistry

- Did applicant request categorical exclusion for environmental assessment?  YES X  NO □
  If no, did applicant submit a complete environmental assessment?  YES □  NO □
  If EA submitted, consulted to Florian Zielinski (HFD-357)?  YES □  NO □

- Establishment Evaluation Request (EER) submitted to DMPQ? No EER requested  YES X
  need for this efficacy supp (per David Lewis, ONDQA PAL, as there were no changes to
  this drugs manufacturing facility as a result of this efficacy supplement.

- If a parenteral product, consulted to Microbiology Team (HFD-805)?  N/A X  NO □
ATTACHMENT

MEMO OF FILING MEETING

DATE: 02/13/06

BACKGROUND:
(Provide a brief background of the drug, e.g., it is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES:

ASSIGNED REVIEWERS (including those not present at filing meeting):

<table>
<thead>
<tr>
<th>Discipline</th>
<th>Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical:</td>
<td>Nancy Snow, M.D.</td>
</tr>
<tr>
<td>Secondary Medical:</td>
<td>N/A</td>
</tr>
<tr>
<td>Statistical:</td>
<td>N/A</td>
</tr>
<tr>
<td>Pharmacology:</td>
<td>NA</td>
</tr>
<tr>
<td>Statistical Pharmacology:</td>
<td>Milton Sloan, Ph.D.</td>
</tr>
<tr>
<td>Chemistry:</td>
<td>Tapah Ghosh, Ph.D.</td>
</tr>
<tr>
<td>Environmental Assessment (if needed):</td>
<td>N/A</td>
</tr>
<tr>
<td>Biopharmaceutical:</td>
<td>A DSI consult was determined to not be needed</td>
</tr>
<tr>
<td>Microbiology, sterility:</td>
<td>Melissa Furness</td>
</tr>
<tr>
<td>Microbiology, clinical (for antimicrobial products only):</td>
<td>DDMAC and DMETS</td>
</tr>
<tr>
<td>DSI:</td>
<td></td>
</tr>
<tr>
<td>Regulatory Project Management:</td>
<td></td>
</tr>
<tr>
<td>Other Consults:</td>
<td></td>
</tr>
</tbody>
</table>

Per reviewers, are all parts in English or English translation? YES X NO □

If no, explain:

CLINICAL

• Clinical site inspection needed? YES □ NO X

• Advisory Committee Meeting needed? YES, date if known □

• 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 X YES □ NO □

CLINICAL MICROBIOLOGY N/A X FILE □ REFUSE TO FILE □

STATISTICS N/A X FILE REFUSE TO FILE □

BIOPHARMACEUTICS FILE X REFUSE TO FILE □

• Biopharm. inspection needed? YES □ NO X
PHARMACOLOGY

N/A X FILE

REFUSE TO FILE □

- GLP inspection needed?

YES □ NO X

CHEMISTRY

FILE X

REFUSE TO FILE □

- Establishment(s) ready for inspection?

No inspection needed for this efficacy supp (per David Lewis, ONDQA PAL, as there were no changes to this drugs manufacturing facility as a result of this efficacy supplement.

YES □ NO X

- Microbiology

YES □ NO X

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:

X The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.

X No filing issues have been identified.

☐ Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. ☐ If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.

2. ☐ 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.

3. X Convey document filing issues/no filing issues to applicant by Day 74. Note: 74 day Letter sent to sponsor within PDUFA timeframe.

Melissa Hancock Furness
Regulatory Project Manager, HFD-180

Version: 12/15/04
Appendix A to NDA Regulatory Filing Review

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

(3) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)

(4) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)

(5) 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.)

(6) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).
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. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and 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,” skip to question 4. Otherwise, answer part (b).

   (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)?

   YES ☐ NO ☐

   *(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

   If “Yes,” skip to question 6. Otherwise, answer part (c).

   (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)?

   YES ☐ NO ☐

   If “No,” please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

4. (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,” skip to question 5. Otherwise, answer part (b).

   (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)?

   YES ☐ NO ☐

   *(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

   NOTE: If there is more than one pharmaceutical alternative approved, consult the Director, Division of
Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

If “Yes,” skip to question 6. Otherwise, answer part (c).

(c) Have you conferred with the Director, Division of Regulatory Policy II, ORP?  
YES ☐  NO ☐

If “No,” please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

5. (a) Is there an approved drug product that does not meet the definition of “pharmaceutical equivalent” or “pharmaceutical alternative,” as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product?  
YES ☐  NO ☐

If “No,” skip to question 6.

(b) Is the approved drug product cited as the listed drug?  
YES ☐  NO ☐

6. 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”).

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

8. Is 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 should be refused for filing under 21 CFR 314.101(d)(9)).  
YES ☐  NO ☐

9. Is the rate at which the product’s active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9)).  
YES ☐  NO ☐

10. Are there certifications for each of the patents listed for the listed drug(s)?  
YES ☐  NO ☐

11. 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.)

☐ 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)].


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 vii statement)
Patent number(s):

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):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference?  
  YES ☐  NO ☐

- Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?  
  YES ☐  NO ☐

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?  
  N/A ☐  YES ☐  NO ☐

- Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv))?  
  N/A ☐  YES ☐  NO ☐
13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).
  
  YES ☐  NO ☐

- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.
  
  YES ☐  NO ☐

- EITHER
  
  The number of the applicant's IND under which the studies essential to approval were conducted.

  IND# ____________________  NO ☐

  OR

  A certification that the NDA sponsor provided substantial support for the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

  YES ☐  NO ☐

3. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

  YES ☐  NO ☐
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/s/

Melissa Furness
8/17/2006 04:36:41 PM
CSO
INFORMATION REQUEST LETTER

NDA 21-957

AstraZeneca LP
Attention: George A. Kummeth
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 for Oral Suspension, 20 and 40 mg.

We also refer to your submission dated May 23, 2006 in response to our May 18, 2006 information request.

We are reviewing the clinical pharmacology 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.

In support of NDA 21-95, you submitted results of the following Bioequivalence study:

"A Single-Centre, Open, Randomized, Three-way Crossover Bioequivalence Study Comparing a Pellets Based Sachet Formulation of Esomeprazole with a Commercial Tablet and a Commercial Capsule of Esomeprazole 40 mg following a Single Oral Dose under Fasting Conditions in Healthy Male and Female Subjects"

Based on the SAS transport data file you submitted for this study, the Clinical Pharmacology reviewer's analysis of the bioequivalence data using WinNonlin version 5.1 differed in many instances from the results presented by you in the table below:
<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment</th>
<th>N</th>
<th>GMR</th>
<th>90% CI Lower</th>
<th>90% CI Upper</th>
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<tr>
<td>AUC</td>
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<td>0.93</td>
<td>1.03</td>
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<tr>
<td>AUC&lt;sub&gt;t&lt;/sub&gt;</td>
<td>Sachet/Tablet</td>
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<td>0.89</td>
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<tr>
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<td>94</td>
<td>0.98</td>
<td>0.93</td>
<td>1.03</td>
</tr>
</tbody>
</table>

Among them, and the most notable, was the finding that the lower limit of 90% CI for GMR for C<sub>max</sub> for Sachet/Capsule in the reviewer’s analysis now lies below the 90% CI acceptance limit (0.7943).

Please provide additional detail as to how the 90% CI for this study were determined, i.e. the statistical code used, and any adjustments to the data that were done in arriving at your results. Please be aware that as the Tablet formulation used in this study is not approved in the US, primacy will be given on the capsule data as the appropriate reference formulation in the determination of bioequivalency for the sachet comparison.

If you have any questions, call Giuseppe Randazzo, Regulatory Project Manager, at (301) 796-0980.

Sincerely,

CAPT E. Dennis Bashaw, Pharm.D.
Director, Div. of Clinical Pharmacology-3
Office of Clinical Pharmacology
U.S. Food and Drug Administration
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Dennis Bashaw
7/11/2006 03:35:35 PM
NDA 21-957

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 December 22, 2005, 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, 20 and 40 mg.

We are reviewing the Chemistry, Manufacturing and Controls 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.

Deficiencies

1. The pellets (granules) are defined as delayed release, therefore, please revise the dissolution method to conform to USP <724> Delayed Drug Release (enteric coated) standard.

2. Revise the analytical method for dissolution to include testing for drug release in acid medium with an acceptance criterion.

3. Your proposal for a tolerance of ___ for the fill weight is not acceptable based on the data you provided. Provide justification for your proposal. The filling process tolerance is reported to conform to USP <755> minimum fill and also conform to <905> Uniformity of Dosage unit. Accordingly, revise and validate the tolerance to a tighter specification.

4. Provide the holding times for the esomeprazole pellets used in the stability batches, and include a written statement committing not to exceed the specified holding time for the future production batches.
Comments

1. Figures 3 and 4 of section 3.2.P.2.2 Pharmaceutical Development page 20 of 24, (also 2.3 Quality Overall Summary) show correlation between the different strengths and the dosage forms seem to indicate that the finished dosage forms, the Sachet and Capsule were tested for dissolution. Please clarify the labels for the figures.

2. Please clarify Figure 1 (section P.5.6 Justification of Specification for Drug Product) to indicate the form of the “esomeprazole” tested in the acid stage buffer (e.g., enteric coated pellets, uncoated pellets, etc.).

3. The NDA was submitted with less than the ICH recommended stability data for the drug product. The data submitted does not support the proposed shelf life of . Please update the stability data to support the proposed shelf life to the NDA.

If you have any questions, call Linda Athey, Regulatory Health Project Manager, at (301) 796-2096.

Sincerely,

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Pre-Marketing Assessment Division II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Joyce Korvick
6/5/2006 04:04:22 PM
Page(s) Withheld

✓ Trade Secret / Confidential

Draft Labeling

Deliberative Process

Withheld Track Number: Administrative-2
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Joyce Korvick
4/26/2006 04:50:38 PM
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 for Oral Suspension, 20 and 40 mg.

We are in the process of reviewing the referenced material and have the following comments:

- In your submission, NDA 21-957, on form 356H and in the Dosage and Administration section of the proposed label, you refer to the 20 and 40 mgs strengths of the Nexium® Delayed-Release Oral Suspension. In contrast, in the CMC section of this application, you state "all the strengths (40, 20, mgs) are included in the present application." These additional dosages should be resubmitted when applicable to new proposed indications or dosing strategies. At that time, the acceptability of these additional dosages will be evaluated.

If you have any questions, call Giuseppe Randazzo, Regulatory Project Manager, at (301) 796-0980.

Sincerely,

Joyce Korvick, M.D., M.P.H.
Deputy Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Joyce Korvick
4/10/2006 09:56:48 AM
FILING COMMUNICATION

NDA 21-957

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

Dear Mr. Kummeth:

Please refer to your December 22, 2005 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium® (esomeprazole) Delayed-Release Oral Suspension.

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 February 20, 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 Melissa Hancock Furness, Regulatory Health Project Manager, at (301) 796-0893.

Sincerely,

{See appended electronic signature page}

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

/s/

Brian Strongin
3/6/2006 10:06:14 AM
**ACTION PACKAGE CHECKLIST**

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<th>Application Information</th>
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<tr>
<td>BLA #: 21-957</td>
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<tr>
<td>NDA Supplement #:</td>
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<td>Proprietary Name:</td>
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<tr>
<td>Dosage Form: Oral Suspension</td>
</tr>
<tr>
<td>RPM: Marlene G. Swider</td>
</tr>
</tbody>
</table>

**NDAs:**

- NDA Application Type: 505(b)(1) 505(b)(2)
- Efficacy Supplement: 505(b)(1) 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.)

- List 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.

- 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.**

- Confirmed
- Corrected

**Version: 7/12/06**
### Application Characteristics

**Review priority:**  
- [x] Standard  
- [ ] Priority

Chemical classification (new NDAs only):

**NDAs, BLAs and Supplements:**  
- [ ] Fast Track  
- [ ] Rolling Review  
- [ ] CMA Pilot 1  
- [ ] CMA Pilot 2  
- [ ] Orphan drug designation

**NDAs: Subpart H**  
- [ ] Accelerated approval (21 CFR 314.510)  
- [ ] Restricted distribution (21 CFR 314.520)

**BLAs: Subpart E**  
- [ ] Accelerated approval (21 CFR 601.41)  
- [ ] Restricted distribution (21 CFR 601.42)

**Subpart I**  
- [ ] Approval based on animal studies

**NDAs and NDA Supplements:**  
- [ ] OTC drug

**Other:**  
- Approval based on bioequivalency studies

**Other comments:**

### Application Integrity Policy (AIP)

- **Applicant is on the AIP**
  - [ ] Yes  
  - [ ] No

- **This application is on the AIP**
  - Exception for review *(file Center Director’s memo in Administrative Documents section)*  
  - [ ] Yes  
  - [ ] No
  - OC clearance for approval *(file communication in Administrative Documents section)*  
  - [ ] Yes  
  - [ ] No  
  - [ ] Not an AP action

### Public communications (approvals only)

- **Office of Executive Programs (OEP) liaison has been notified of action**  
  - [x] Yes  
  - [ ] No

- **Press Office notified of action**
  - [x] Yes  
  - [ ] No
  - [ ] None  
  - [ ] FDA Press Release  
  - [ ] FDA Talk Paper  
  - [ ] CDER Q&As  
  - [ ] Other

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Version: 7/12/2006
### Exclusivity

- **NDAs: Exclusivity Summary (approvals only)** *(file Summary in Administrative Documents section)*
  - Included

- **Is approval of this application blocked by any type of exclusivity?**
  - **NDAs/BLAs:** Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? 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.
  - **NDAs:** Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*
  - **NDAs:** Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*
  - **NDAs:** Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*

### Patent Information (NDAs and NDA supplements only)

- **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.
  - Verified
  - Not applicable because drug is an old antibiotic.

- **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.
  - 21 CFR 314.50(i)(1)(i)(A)
    - Verified
  - 21 CFR 314.50(i)(1)(ii)
    - (ii)
    - (iii)
    - No paragraph III certification
    - Date patent will expire

- **[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). *(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).*
  - N/A (no paragraph IV certification)
  - Verified

- **[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.

  Answer the following questions for each paragraph IV certification:

  1. Have 45 days passed since the patent owner’s receipt of the applicant’s
  - Yes
  - No

Version: 7/12/2006
notice of certification?

(Note: The date that the patent owner received the applicant’s notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If “Yes,” skip to question (4) below. If “No,” continue with question (2).

(2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant’s notice of certification, as provided for by 21 CFR 314.107(f)(3)?

If “Yes,” 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).

If “No,” continue with question (3).

(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If “No,” the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

(4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

If “Yes,” 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).

If “No,” continue with question (5).

(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner’s receipt of the applicant’s notice of certification?

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced.
within the 45-day period).

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).

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.

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<tr>
<td>BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)</td>
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<tr>
<td>- Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)</td>
<td>10/17/06</td>
</tr>
<tr>
<td>- Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</td>
<td></td>
</tr>
<tr>
<td>- Original applicant-proposed labeling</td>
<td>12/33/05</td>
</tr>
<tr>
<td>- Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</td>
<td>PRILOSEC, PREVACID, PROTONIX</td>
</tr>
<tr>
<td>Patient Package Insert</td>
<td></td>
</tr>
<tr>
<td>- Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)</td>
<td>N/A</td>
</tr>
<tr>
<td>- Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</td>
<td></td>
</tr>
<tr>
<td>- Original applicant-proposed labeling</td>
<td></td>
</tr>
<tr>
<td>- Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</td>
<td></td>
</tr>
<tr>
<td>Medication Guide</td>
<td></td>
</tr>
<tr>
<td>- Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)</td>
<td>N/A</td>
</tr>
<tr>
<td>- Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</td>
<td></td>
</tr>
<tr>
<td>- Original applicant-proposed labeling</td>
<td></td>
</tr>
<tr>
<td>- Other relevant labeling (e.g., most recent 3 in class, class labeling)</td>
<td></td>
</tr>
<tr>
<td>Labels (full color carton and immediate-container labels)</td>
<td></td>
</tr>
<tr>
<td>- Most recent division-proposed labels (only if generated after latest applicant submission)</td>
<td>12/22/05</td>
</tr>
<tr>
<td>- Most recent applicant-proposed labeling</td>
<td></td>
</tr>
<tr>
<td>Labeling reviews and minutes of any labeling meetings (indicate dates of reviews and meetings)</td>
<td>DMETS 9/22/06, DSRCS, DDMAC 10/12/06; 9/26/06, SEALD, Other reviews, Memos of Mtgs</td>
</tr>
</tbody>
</table>
### Administrative Documents

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administrative Reviews</td>
<td>RPM Filing Review/Memo of Filing Meeting; ADRA</td>
<td>2/13/06</td>
</tr>
<tr>
<td>NDA and NDA supplement approvals only</td>
<td>Exclusivity Summary (signed by Division Director)</td>
<td>Included</td>
</tr>
<tr>
<td>AIP-related documents</td>
<td>Center Director’s Exception for Review memo</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If AP: OC clearance for approval</td>
<td></td>
</tr>
<tr>
<td>Pediatric Page</td>
<td>(all actions)</td>
<td>Included</td>
</tr>
<tr>
<td>Department certification (original applications only)</td>
<td>verified that qualifying language was not used in certification and that certifications from foreign applicants are consigned by U.S. agent. (Include certification.)</td>
<td>Verified, statement is acceptable</td>
</tr>
<tr>
<td>Postmarketing Commitment Studies</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Outgoing Agency request for post-marketing commitments (if located elsewhere in package, state where located)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Incoming submission documenting commitment</td>
<td></td>
</tr>
<tr>
<td>Outgoing correspondence</td>
<td>letters including previous action letters, emails, faxes, telecons</td>
<td>X</td>
</tr>
<tr>
<td>Internal memoranda, telecons, email, etc.</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Minutes of Meetings</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pre-Approval Safety Conference (indicate date; approvals only)</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Pre-NDA/BLA meeting (indicate date)</td>
<td>No mtg</td>
</tr>
<tr>
<td></td>
<td>EOP2 meeting (indicate date)</td>
<td>No mtg</td>
</tr>
<tr>
<td></td>
<td>Other (e.g., EOP2a, CMC pilot programs)</td>
<td>N/A</td>
</tr>
<tr>
<td>Advisory Committee Meeting</td>
<td></td>
<td>No AC meeting</td>
</tr>
<tr>
<td></td>
<td>Date of Meeting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>48-hour alert or minutes, if available</td>
<td></td>
</tr>
<tr>
<td>Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)</td>
<td></td>
<td></td>
</tr>
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</table>

### CMC/Product Quality Information

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
<th>Date/Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMC/Product review(s)</td>
<td>(indicate date for each review)</td>
<td>10/20/06; 10/16/06</td>
</tr>
<tr>
<td>Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer</td>
<td>(indicate date for each review)</td>
<td>None</td>
</tr>
<tr>
<td>BLAs: Product subject to lot release (APs only)</td>
<td></td>
<td>Yes  No</td>
</tr>
<tr>
<td>Environmental Assessment</td>
<td>(check one)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</td>
<td>See CMC Review dated 10/16/06</td>
</tr>
<tr>
<td></td>
<td>Review &amp; FONSI (indicate date of review)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Review &amp; Environmental Impact Statement (indicate date of each review)</td>
<td></td>
</tr>
<tr>
<td>NDAs: Microbiology reviews (sterility &amp; pyrogenicity)</td>
<td>(indicate date of each review)</td>
<td>Not a parenteral product</td>
</tr>
<tr>
<td>Facilities Review/Inspection</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NDAs: Facilities inspections (include EER printout)</td>
<td>Date completed:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acceptable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Withhold recommendation</td>
</tr>
</tbody>
</table>

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### BLAs: Facility-Related Documents
- Facility review *(indicate date(s))*
- Compliance Status Check (approvals only, both original and supplemental applications) *(indicate date completed, must be within 60 days prior to AP)*

<table>
<thead>
<tr>
<th>Status</th>
<th>Requested</th>
<th>Accepted</th>
<th>Hold</th>
</tr>
</thead>
</table>

### NDAs: Methods Validation

<table>
<thead>
<tr>
<th>Status</th>
<th>Completed</th>
<th>Requested</th>
<th>Not yet requested</th>
<th>Not needed</th>
</tr>
</thead>
</table>

### Nonclinical Information

- Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*
  - N/A
- Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*
  - None
- Statistical review(s) of carcinogenicity studies *(indicate date for each review)*
  - No canc
- ECAC/CAC report/memo of meeting
- Nonclinical inspection review Summary (DSI)
  - None requested

### Clinical Information

- Clinical review(s) *(indicate date for each review)*
  - 9/11/06
- Financial Disclosure review(s) or location/date if addressed in another review
  - See MO review dated 9/11/06
- Clinical consult reviews from other review disciplines/divisions/Centers *(indicate date of each review)*
  - None
- Microbiology (efficacy) review(s) *(indicate date of each review)*
  - Not needed
- Safety Update review(s) *(indicate location/date if incorporated into another review)*
  - N/A
- Risk Management Plan review(s) *(indicate date of each review)*
  - N/A
- Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date of each review)*
  - Not needed
- DSI Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*
  - None requested
  - Clinical Studies
  - Bioequivalence Studies
  - Clin Pharm Studies
- Statistical Review(s) *(indicate date for each review)*
  - None
- Clinical Pharmacology review(s) *(indicate date for each review)*
  - None 10/5/06

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Appendix A to Action Package Checklist

An NDA or NDA supplemental 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. Or 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.
3. Or 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. And 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.
3. And 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. Or 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.
3. Or 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.

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