CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-056

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

NDA 22-056

PRILOSEC® (omeprazole magnesium)
For Delayed-Release Oral Suspension

New Drug Application

1.3.5.1 Patent Information

Department of Health and Human Services
Food and Drug Administration

PATENT INFORMATION SUBMITTED WITH THE ILING 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

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
See OMB Statement on Page 3.

NDA NUMBER
22-056

NAME OF APPLICANT / NDA HOLDER
AstraZeneca LP

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

TRADE NAME (OR PROPOSED TRADE NAME)
PRILOSEC® (omeprazole magnesium) Delayed-Release Oral Suspension

ACTIVE INGREDIENT(S)	STRENGTH(S)
Omeprazole Magnesium	2.5 mg and 10 mg omeprazole (present as omeprazole magnesium)

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.

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

1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
4,786,505	11/22/1988	4/20/2007

d. Name of Patent Owner
AB Hässle

Address *(of Patent Owner)*
SE-431 83

City/State
Mölndal, Sweden

ZIP Code	FAX Number *(if available)*
SE-431 83	
Telephone Number	**E-Mail Address *(if available)***
01146317761000	

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, Policy, Legal & Scientific
Affairs & General Counsel
AstraZeneca Pharmaceuticals LP

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

City/State
Wilmington, DE

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

the patent referenced above a patent that has been submitted previously for the proved 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.

rug Substance (Active Ingredient)

	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
	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)* 10	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 PRILOSEC For Delayed-Release Oral Suspension Proposed Label at INDICATIONS AND USAGE and DOSAGE AND ADMINISTRATION.	

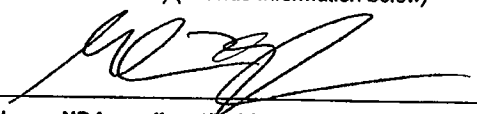
5. No Relevant Patents

	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)*	Date Signed
	12/2/06

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

Check applicable box and provide information below.

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

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

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
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NDA NUMBER
22-056

NAME OF APPLICANT / NDA HOLDER
AstraZeneca LP

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

1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
4,853,230	8/1/1989	4/20/2007

d. Name of Patent Owner	Address *(of Patent Owner)*	
AB Hässle	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 (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address *(of agent or representative named in 1.e.)*	
☞ Vice President, Policy, Legal & Scientific Affairs & General Counsel AstraZeneca Pharmaceuticals LP	1800 Concord Pike	
	City/State: Wilmington, DE	
	ZIP Code: 19803	FAX Number *(if available)*
	Telephone Number: (800) 456-3669	E-Mail Address *(if available)*

the patent referenced above a patent that has been submitted previously for the proved NDA or supplement referenced above? ☐ Yes ☒ No

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.

Drug Substance (Active Ingredient)

	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
	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)* 13	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 PRILOSEC For Delayed-Release Oral Suspension Proposed Label at INDICATIONS AND USAGE and 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

Declaration Certification

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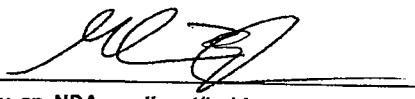
6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide Information below)*	Date Signed
	12/2/06

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

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

Department of Health and Human Services
Food and Drug Administration

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AstraZeneca LP

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ACTIVE INGREDIENT(S)	STRENGTH(S)
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1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
5,690,960	11/25/1997	11/25/2014

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)*

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, Policy, Legal & Scientific Affairs & General Counsel
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

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	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
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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
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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
	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

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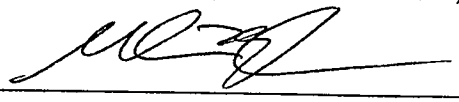	12/2/06

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

Department of Health and Human Services
Food and Drug Administration

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a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
5,900,424	5/4/1999	5/4/2016

d. Name of Patent Owner
AstraZeneca AB

Address *(of Patent Owner)*
SE-151 85

City/State
Södertälje, Sweden

ZIP Code	FAX Number *(if available)*
SE-151 85	

Telephone Number	E-Mail Address *(if available)*
01146855326000	

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, Policy, Legal & Scientific Affairs & General Counsel
AstraZeneca Pharmaceuticals LP

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

City/State
Wilmington, DE

ZIP Code	FAX Number *(if available)*
19803	

Telephone Number	E-Mail Address *(if available)*
(800) 456-3669	

the patent referenced above a patent that has been submitted previously for the proved 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.

rug Substance (Active Ingredient)

	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? * 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.	☐ 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

rug Product (Composition/Formulation)

	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)* 21, 22	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 PRILOSEC For Delayed-Release Oral Suspension Proposed Label at INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, and CLINICAL PHARMACOLOGY, Pharmacodynamics.	

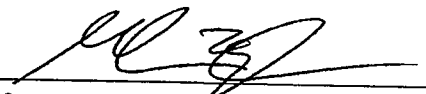
5. No Relevant Patents

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 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)*	Date Signed
	12/2/06

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

Check applicable box and provide information below.

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

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

Department of Health and Human Services
Food and Drug Administration

PATENT INFORMATION SUBMITTED WITH THE ILING 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

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
See OMB Statement on Page 3.

NDA NUMBER
22-056

NAME OF APPLICANT / NDA HOLDER
AstraZeneca LP

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

TRADE NAME (OR PROPOSED TRADE NAME)
PRILOSEC® (omeprazole magnesium) Delayed-Release Oral Suspension

ACTIVE INGREDIENT(S)
Omeprazole Magnesium

STRENGTH(S)
2.5 mg and 10 mg omeprazole (present as omeprazole magnesium)

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.

each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the rmation described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, omplete 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, Policy, Legal & Scientific Affairs & General Counsel
AstraZeneca Pharmaceuticals LP

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

City/State
Wilmington, DE

ZIP Code
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FAX Number *(if available)*

Telephone Number
(800) 456-3669

E-Mail Address *(if available)*

the patent referenced above a patent that has been submitted previously for the pproved 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)

	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
	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)* 11	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 PRILOSEC For Delayed-Release Oral Suspension Proposed Label at INDICATIONS AND USAGE and DOSAGE AND ADMINISTRATION.	

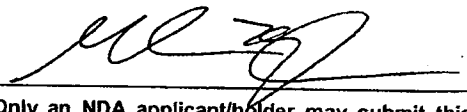
5. No Relevant Patents

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)*	Date Signed
	12/2/06

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

Check applicable box and provide information below.

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

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

EXCLUSIVITY SUMMARY

NDA # 22-056 SUPPL # N/A HFD # 180

Trade Name Prilosec For Delayed Release Oral Suspension

Generic Name Omeprazole

Applicant Name AstraZeneca

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES ☒ NO ☐

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

505(b)(1)

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

YES ☒ NO ☐

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

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

d) Did the applicant request exclusivity?

YES ☒ NO ☐

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

3 Years

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

YES ☒ NO ☐

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

Yes; however, supplement 19-810/S074 was approved prior to the submission of this NDA. The current NDA 22-056 was submitted in response to the Post Marketing Commitment requesting development of an age appropriate formulation.

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

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

YES ☐ NO ☒

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES ☒ NO ☐

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

NDA# 19-810 Prilosec Delayed-Released Capsules

NDA# 21-636 Zegerid

NDA# ** See attached table for additional NDA #'s

2. Combination product.

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

YES ☐ NO ☐

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

NDA#

NDA#

NDA#

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

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

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

summary for that investigation.

YES ☒ NO ☐

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

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

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

YES ☐ NO ☐

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

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

YES ☐ NO ☐

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

YES ☐ NO ☐

If yes, explain:

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

YES ☐ NO ☐

If yes, explain:

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

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

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

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

Investigation #1	YES ☐	NO ☒
Investigation #2	YES ☐	NO ☐

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

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

Investigation #1	YES ☐	NO ☒
Investigation #2	YES ☐	NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a

similar investigation was relied on:

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

Study 251: A Multicenter, Randomized, Single-Blind Study to Evaluate Omeprazole for the Treatment of Clinically Diagnosed Gastroesophageal Reflux Disease (GERD) in Pediatric Patients Ages 0 months through 24 months, Inclusive

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

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

Investigation #1		!
		!
IND # 23,284	YES ☒	! NO ☐
		! Explain:
Investigation #2		!
		!
IND #	YES ☐	! NO ☐
		! Explain:

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

Investigation #1 !

YES ☐	! 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: Elizabeth A.S. Ford, R.N.
Title: Regulatory Health Project Manager
Date: 3/13/2008

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

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

NDA #	21689	Nexium IV
NDA #	21706	Zegerid Powder 40mg
NDA #	21849	Zegerid 20/40mg Capsule
NDA #	21850	Zegerid 20/40mg Chewable Tablet
NDA #	21957	Nexium Delayed-Release Granules for Oral
NDA #	22101	Nexium

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
3/20/2008 04:36:42 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 22-056 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: January 15, 2008 (Class I resubmission) PDUFA Goal Date: March 14, 2008

HFD 180 Trade and generic names/dosage form: Prilosec (omeprazole) 2.5 and 10 mg Delayed Release Granules for Oral Suspension

Applicant: Astra Zeneca Therapeutic Class: Proton Pump Inhibitor

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 th e next question.
- ☐ No. PREA does not apply. Skip to signature block.

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

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

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

Number of indications for this application(s): 2

Indication #1: Short-term treatment of pediatric patients with Gastroesophageal Reflux Disease (GERD)

Is this an orphan indication?

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

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

- ☐ Yes: Please proceed to Section A.
- ☒ No: Please check all that apply: ____Partial Waiver __X__Deferred __X__Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

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

Min_____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____
Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

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

Min _____ kg_____ mo._____ yr.__0__ Tanner Stage_____
Max_____ kg_____ mo._____ yr.__1__ Tanner Stage_____

Reason(s) for deferral:

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

Other: Formulation is ready for approval in other age groups.

Date studies are due (mm/dd/yy): 12/31/2010

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

Section D: Completed Studies

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

Min ____ kg_____ mo._____ yr.__1__ Tanner Stage_____
Max____ kg_____ mo._____ yr.__2__ Tanner Stage_____

Comments:

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

This page was completed by:

(See appended electronic signature page)

Regulatory Project Manager

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

(Revised: 10/10/2006)

Attachment A

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

Indication #2: Erosive Esophagitis

Is this an orphan indication?

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

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

- ☐ **Yes: Please proceed to Section A.**
- ☒ **No: Please check all that apply: ____Partial Waiver __X__Deferred _X__Completed**
  NOTE: More than one may apply
  Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

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

Min _____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

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

Min _____ kg_____ mo._____ yr.__0___ Tanner Stage_____
Max_____ kg_____ mo._____ yr.__1___ Tanner Stage_____

Reason(s) for deferral:

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

Date studies are due (mm/dd/yy): 12/31/2010

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

Section D: Completed Studies

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

Min _____ kg_____ mo._____ yr.__1___ Tanner Stage_____
Max_____ kg_____ mo._____ yr.__2___ Tanner Stage_____

Comments: *10 mg P.O. once daily for up to 8 weeks

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

This page was completed by:

(See appended electronic signature page)

Regulatory Project Manager

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

(Revised: 10/10/2006)

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/s/

Elizabeth A Ford
3/19/2008 06:33:57 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : NDA 22-056 Supplement Type (e.g. SE5): N/A Supplement Number: N/A

Stamp Date: 12/20/06 PDUFA Goal Date: 10/20/07

HFD 180 Trade and generic names/dosage form: Prilosec (omeprazole magnesium) for Delayed-Release Oral Suspension

Applicant: AstraZeneca LP Therapeutic Class: Proton Pump Inhibitors

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

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

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

Indication(s) *previously approved* (please complete this section for supplements only): N/A

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

Number of indications for this application(s): 2

Indication #1: Treatment of Gastroesophageal Reflux Disease

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 __X__Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

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

Min_____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____
Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

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

Min _____ kg_____ mo._____ yr. Birth Tanner Stage_____
Max_____ kg_____ mo._____ yr. 16 years Tanner Stage_____

Reason(s) for deferral:

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

Other:_____

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 DFS.

Section D: Completed Studies

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

Min _____ kg_____ mo._____ yr. Birth Tanner Stage_____
Max_____ kg_____ mo._____ yr. 16 years Tanner Stage_____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

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

(Revised: 10/10/2006)

Attachment A

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

Indication #2: _____ **healing of erosive esophagitis** b(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 ____Deferred __X__Completed**
  NOTE: More than one may apply
  Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

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

Min _____ **kg**_____ **mo.**_____ **yr.**_____ **Tanner Stage**_____
Max_____ **kg**_____ **mo.**_____ **yr.**_____ **Tanner Stage**_____

Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

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

Min _____ kg_____ mo._____ 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**
- ☐ **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 DFS.

:tion D: Completed Studies

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

Min _____ kg_____ mo._____ yr. Birth Tanner Stage_____
Max_____ kg_____ mo._____ yr. 16 years Tanner Stage_____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

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

(Revised: 10/10/2006)

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/s/

Brian Strongin
10/18/2007 04:58:09 PM

1.3.3 Debarment Certification

ITEM 16 DEBARMENT CERTIFICATION

Re: NDA 22-056

PRILOSEC® (omeprazole magnesium) for 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, that we did not use and will not use in connection with this New Drug Application for PRILOSEC® (omeprazole magnesium) for Delayed-Release Oral Suspension, NDA 22-056 (Study Number D9586C00002), the services of any person in any capacity debarred under section 306 (a) or (b).

Sincerely,

Donna Dea, Vice President
Regulatory Affairs
AstraZeneca LP

MEMORANDUM OF TELECON

DATE: March 20, 2008, 3:45 PM

APPLICATION NUMBER: NDA 22-056

BETWEEN:

Name: George Kummeth
Phone: 610-805-6225
Representing: AstraZeneca LP

AND

Name: Joyce Korvick, M.D.
Deputy Director
Division of Gastroenterology Products, HFD-180

Elizabeth Ford, R.N.
Regulatory Health Project Manager
Division of Gastroenterology Products, HFD-180

SUBJECT: NDA 22-056/Prilosec: Pediatric Research Equity Act (PREA) and deferral of Pediatric Study for pediatric patients ages birth to 1 year.

Following a discussion regarding Pediatric Research Equity Act (PREA), and the recommendations of the Pediatric Review Committee regarding NDA 22-056, Prilosec (omeprazole) For Delayed-Release Oral Suspension, AstraZeneca agreed to a deferred post marketing commitment (PMC) for the study in ages birth to 1 year for the treatment of GERD and erosive esophagitis, with final report submission due by December 31, 2010.

b(4)

[redacted] and then initiate discussions with the FDA on potential approaches to fulfill the PMC for NDA 22-056, or request a waiver. Further discussions with the FDA will be requested through a formal meeting request.

Elizabeth A.S. Ford, R.N.
Regulatory Health Project Manager

Initialed: JK 3/25/08

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use NEXIUM safely and effectively. See full prescribing information for NEXIUM.

NEXIUM (esomeprazole magnesium) DELAYED-RELEASE CAPSULES
NEXIUM (esomeprazole magnesium) FOR DELAYED-RELEASE ORAL SUSPENSION
Initial U.S. Approval: 1989 (omeprazole)

----------INDICATIONS AND USAGE----------

NEXIUM is a proton pump inhibitor indicated for the following:

- Treatment of gastroesophageal reflux disease (GERD) (1.1)
- Risk reduction of NSAID-associated gastric ulcer (1.2)
- *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence (1.3)
- Pathological hypersecretory conditions, including Zollinger-Ellison syndrome (1.4)

----------DOSAGE AND ADMINISTRATION----------

Indication	Dose	Frequency
Gastroesophageal Reflux Disease (GERD)		
Adults	20 mg or 40 mg	Once daily for 4 to 8 weeks
12 to 17 years	20 mg or 40 mg	Once daily for up to 8 weeks
1 to 11 years	10 mg or 20 mg	Once daily for up to 8 weeks
Risk Reduction of NSAID-Associated Gastric Ulcer		
	20 mg or 40 mg	Once daily for up to 6 months
***H. pylori* Eradication** *(Triple Therapy):*		
NEXIUM	40 mg	Once daily for 10 days
Amoxicillin	1000 mg	Twice daily for 10 days
Clarithromycin	500 mg	Twice daily for 10 Days
Pathological Hypersecretory Conditions		
	40 mg	Twice daily

See full prescribing information for administration options (2)

----------DOSAGE FORMS AND STRENGTHS----------

- NEXIUM Delayed-Release Capsules, 20 mg and 40 mg (3)
- NEXIUM For Delayed-Release Oral Suspension, 10 mg, 20 mg, and 40 mg (3)

----------CONTRAINDICATIONS----------

Patients with known hypersensitivity to any component of the formulation or to substituted benzimidazoles (angioedema and anaphylaxis have occurred) (4)

----------WARNINGS AND PRECAUTIONS----------

- Symptomatic response does not preclude the presence of gastric malignancy (5.1)
- Atrophic gastritis has been noted with long-term omeprazole therapy (5.2)
- Triple therapy for *H. pylori* – there are risks due to the antibiotics; see separate prescribing information for individual antibiotics (5.3, 5.4)

----------ADVERSE REACTIONS----------

Most common adverse reactions:
Adult (≥ 18 years) use (incidence ≥ 1%):

- Headache, diarrhea, nausea, flatulence, abdominal pain, constipation, and dry mouth (6.1)

Pediatric (1 - 17 years) use (incidence ≥ 1-2%):

- Headache, diarrhea, abdominal pain, nausea, and somnolence (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- May affect plasma levels of antiretroviral drugs – use with atazanavir and nelfinavir is not recommended; if saquinavir is used with NEXIUM, monitor for toxicity and consider saquinavir dose reduction (7.1)
- May interfere with drugs for which gastric pH affects bioavailability (e.g., ketoconazole, iron salts, and digoxin) (7.2)
- Combined inhibitor of CYP 2C19 and 3A4 may raise esomeprazole levels (7.3)

----------USE IN SPECIFIC POPULATIONS----------

- Severe liver impairment – do not exceed dose of 20 mg (2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labelling.

REVISED 6/2009

FULL PRESCRIBING INFORMATION: CONTENTS

*Sections or subsections omitted from the full prescribing information are not listed.

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/s/

Elizabeth A Ford
3/26/2008 10:58:08 AM
CSO

MEMORANDUM OF TELECON

DATE: March 11, 2008, 12:30 PM

APPLICATION NUMBER: NDA 22-056

BETWEEN:

Name: George Kummeth, Doug Levine, Kelly Davis, Myrlene Macera
Phone: 888-390-0676, Passcode 28479
Representing: AstraZeneca LP

AND

Name: Joyce Korvick, M.D., DD, Division of Gastroenterology Products (DGP)
Wen Yi Gao, M.D., MO, DGP
Nancy Snow, M.D., Acting MOTL, DGP
Brian Strongin, R.Ph., MBA, CPMS
Elizabeth Ford, R.N., RPM,

SUBJECT: NDA 22-056/Prilosec: Labeling Negotiations

BACKGROUND: NDA 22-056, Prilosec (omeprazole) provides for an oral age appropriate formulation of omeprazole - For Delayed-Release Oral Suspension. Prilosec sachets were developed to fulfill the post-marketing commitment to develop an age-appropriate formulation for pediatric patients 0 to 2 years of age, issued by the Agency in the 12 July 2002 Approval letter for supplement NDA 19-810/S074, which provided for pediatric labeling for ages 2 to 16 years for Prilosec. An approvable letter was issued to NDA 22-056 on 19 October 2007. For approval, the sponsor was required to submit draft labeling revised in response to the 18 October 2007 communication, and submit a safety update. A complete response to the 19 October 2007 approvable letter was received on 15 January 2008.

Following the SEALD and Clinical reviews, concerns were identified regarding the scope of the new indications claimed and the age groups identified by the NDA submission. Specifically, AstraZeneca proposed taking the current indications for GERD and extending them to 0 years of age. Given Study 251 of NDA 22-056, which included one patient less than 1 month old, 92 patients 1- 11 months of age, and 10 patients 11-24 months of age, the suggestion was raised to approve this new formulation in pediatric patients greater than one year of age. An internal meeting between DGP team members and the PEDS staff took place on 7 March 2008. At this meeting, the pediatric team agreed with these concerns, and with the suggestion of approving the proposed indication for pediatric patients greater than one year of age.

TODAY'S CALL

The teleconference between AstraZeneca and the FDA was scheduled to discuss the proposed package insert, and to convey the aforementioned issues to the sponsor.

Following a discussion of the SEALD review, and the above-mentioned concerns regarding the indications and age group targeted by the proposed formulation, the sponsor agreed to revise the proposed package insert to reflect the formatting of the recently approved Nexium (esomeprazole magnesium) package insert (NDA 22-101) following the Physician Labeling Rule and references to pediatric patients under 1 year of age.

The current proposed label with the marked FDA revisions will be sent to the sponsor as a guide, but the sponsor understood this marked label does not represent the final recommendations of the Agency. The sponsor agreed to submit a revised label to the Agency for review.

Elizabeth A.S. Ford, R.N.
Regulatory Health Project Manager

Reviewed/Initialed: BKS 3/25/08, WYG 3/25/08, JK 3/25/08

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/s/

Elizabeth A Ford
3/26/2008 10:57:24 AM
CSO

MEMORANDUM OF TELECON

DATE: March 19, 2008, 3:45 PM

APPLICATION NUMBER: NDA 22-056

BETWEEN:

Name: George Kummeth, Doug Levine, Kelly Davis,
Phone: 888-790-1962, Passcode 35324
Representing: AstraZeneca LP

AND

Name: Joyce Korvick, M.D., DD, Division of Gastroenterology Products (DGP)
Wen Yi Gao, M.D., MO, DGP
Elizabeth Ford, R.N., RPM,

SUBJECT: NDA 22-056/Prilosec: Labeling Negotiations

BACKGROUND: In a March 11, 2008 teleconference between the FDA and AstraZeneca, AstraZeneca agreed to revise, and submit to the FDA for review, the proposed Prilosec package insert to reflect harmony with the formatting of the recently approved Nexium (esomeprazole magnesium) package insert (NDA 22-101) following the Physician Labeling Rule and in addition b(4)

After conferring with Dr. Joyce Korvick, DGP Deputy Director, I relayed to Mr. Kummeth that the PeRC agreed with DGP to allow the efficacy of > 1year olds in the label. b(4)

TODAY'S CALL

On March 18, 2008, AstraZeneca submitted a revised Prilosec package insert for NDA 22-056 for review by the FDA. The teleconference on March 19, 2008 was scheduled to discuss additional revisions to the label submitted on March 18, 2008.

Additional revisions to the package insert conveyed to the sponsor included:

1. Minor editorial comments
2. b(4)

3. b(4)

The FDA-marked label will be sent to the sponsor for review and comment for any additional editorial revisions.

Elizabeth A.S. Ford, R.N.
Regulatory Health Project Manager

Reviewed/Initialed: BKS 3/25/08, WYG 3/25/08, JK 3/25/08

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/s/

Elizabeth A Ford
3/26/2008 10:57:43 AM
CSO

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: March 19, 2008

To: George A. Kummeth, Global Director	**From:** Elizabeth A.S. Ford, RN
Company: AstraZeneca	Division of Gastroenterology Products
Fax number: 302-886-2822	**Fax number:** 301-796-9905
Phone number: 302-885-8414	**Phone number:** 301-796-0193

Subject: NDA 22-056 Prilosec (omeprazole) 2.5mg and 10mg Delayed Release Granules for Oral Suspension

Total no. of pages including cover: 2

Comments: As per our Teleconference today, here are the suggestions for the label. Please note the comment on page 10, last paragraph in section 6.1, line 5.

Document to be mailed: ☐ YES ☑ NO

39 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

__X__ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Administrative- 5

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/s/

Elizabeth A Ford
3/19/2008 06:12:55 PM
CSO

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: March 11, 2008

To: George A. Kummeth, Global Director	**From:** Elizabeth A.S. Ford, RN
Company: AstraZeneca	Division of Gastroenterology Products
Fax number: 302-886-2822	**Fax number:** 301-796-9905
Phone number: 302-885-8414	**Phone number:** 301-796-0193

Subject: NDA 22-056 Prilosec (omeprazole) 2.5mg and 10mg Delayed Release Granules for Oral Suspension

Total no. of pages including cover: 2

Comments: As per our Teleconference today, here are the suggestions for the label. In addition, please edit the pediatric sections per the teleconference discussion today.

Document to be mailed: ☐ YES ☑ NO

38 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

__X__ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Administrative- 3

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/s/

Elizabeth A Ford
3/11/2008 05:41:18 PM
CSO

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: February 21, 2008

To: George A. Kummeth, Global Director	**From:** Elizabeth A.S. Ford, RN
Company: AstraZeneca	Division of Gastroenterology Products
Fax number: 302-886-2822	**Fax number:** 301-796-9905
Phone number: 302-885-8414	**Phone number:** 301-796-0193

Subject: NDA 22-056 Prilosec (omeprazole) 2.5mg and 10mg Delayed Release Granules for Oral Suspension: Language Regarding Atazanavir Drug-Drug Interaction

Total no. of pages including cover: 2

Comments: Please see our proposed language for the Atazanavir Drug-Drug Interaction.

Document to be mailed: ☐ YES ☑ NO

1 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

__X__ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Administrative- 4

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/s/

Elizabeth A Ford
2/26/2008 07:14:53 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-056

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

Dear Mr. Kummeth:

We acknowledge receipt on January 15, 2008 of your January 14, 2008 resubmission to your new drug application for Prilosec (omeprazole) 2.5mg and 10mg Delayed Release Granules for Oral Suspension.

We consider this a complete, class 1 response to our October 19, 2007 action letter. Therefore, the user fee goal date is March 14, 2008.

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

If you have any question, call Elizabeth Ford, Regulatory Project Manager, at (301) 796-0193.

Sincerely,

[See appended electronic signature page]

Elizabeth A. S. Ford, RN
Regulatory Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Elizabeh A Ford
1/25/2008 11:31:07 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-056

INFORMATION REQUEST LETTER

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

Dear Mr. Kummeth:

Please refer to your December 20, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec (omeprazole magnesium) for Delayed-Release Oral Suspension.

We are reviewing the labeling 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.

I. GENERAL COMMENTS

A. We recommend moving much of the data on the use of Prilosec in pediatric patients from its current placement in the label. Because Prilosec is approved for pediatric use in certain conditions, the discussion of the pediatric data should appear in the same places throughout the label as is done for the adult data (e.g., pediatric clinical studies should appear in Clinical Studies, pediatric safety data should be in Adverse Reactions, pediatric pharmacokinetic data should be in Pharmacokinetics). The section "8.4 Pediatric Use" should summarize the available pediatric data upon which the approval was based, and cross-reference the detailed discussions elsewhere in the label. This section should also summarize any important differences noted between pediatric and adult patients that are relevant for the clinician.

B. We recommend rearranging some of the information about the use of clarithromycin and amoxicillin in the label. Specifically, the contraindications about these two drugs should not be included in the Prilosec label's contraindications section, and the warnings/precautions discussions should be modified. There should be a warning/precaution about combination use with clarithromycin, including all the relevant information, and another one for combination use with amoxicillin. There would also be the warnings/precautions that are specific to omeprazole (i.e., those currently under section 5.3). The topics in this section should be presented in decreasing order of importance, with the most important coming first. Once the ordering of this section has

been determined, then a decision must be made regarding how many of them warrant inclusion in Highlights. All may be included, or just the most important ones.

C. The section "Recent Major Changes" in Highlights should reflect changes to the Indications and Usage section (the new approved patient population of children ~2) and Dosage and Administration (dosing recommendations in this same population). The text in the FPI that corresponds to these changes must have a vertical line inserted in the left margin next to the new information. b(4

D. Since the labeling change from April 2007 provided for the addition of a new drug interaction, this change was not to one of the five sections covered under "Recent Major Changes" (Boxed Warning, Contraindications, Warnings and Precautions, Indications and Usage, and Dosage and Administration). Therefore, it should not be included under "Recent Major Changes" in Highlights. Please ignore the request in our previous letter to add this section.

E. All tables in the label should be titled and consecutively numbered.

II. HIGHLIGHTS

A. Dosage and Administration

This section must include cross-references to the appropriate section of the FPI. We suggest putting the section number (in parentheses) at the end of each indicated condition.

B. Warnings and Precautions

1. As noted above, please revise this section to reflect changes made in the FPI.

2. The preferred presentation in this section is to state the risk followed by a colon, and then any further information and clinical recommendations, as appropriate. Please revise accordingly.

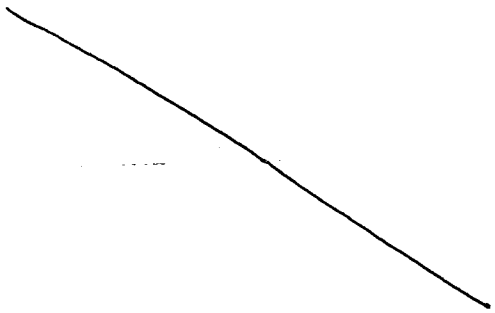
C. Adverse Reactions

This list is longer than is usually seen in Highlights. Please consider using a higher cut-off rate to reduce the list to the 4-6 most common adverse reactions.

D. Drug Interactions

As with Warnings and Precautions, this section should be reformatted to list the drug name (or drug class) followed by a colon, and then a description of the interaction or recommended clinical intervention. The current presentation is too wordy and the critical information is not easily accessible. We suggest:

1.
2.
3.
4.
5.
6.



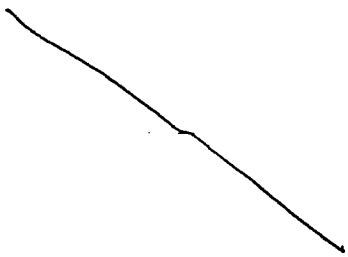
b(4)

III. CONTENTS

A. Once the Full Prescribing Information (FPI) has been finalized, the Contents must be updated to ensure accuracy of the numbering and section titles. Then, any corresponding changes should be made to the Highlights and cross-references throughout the label.

B. If Highlights and Contents cannot fit on one page, we prefer that Contents appear in its entirety on page 2, instead of splitting it between two pages. As with Highlights, the font size of this section can be smaller to enable it to fit on one page.

IV. FULL PRESCRIBING INFORMATION



b(4)

_6_ Page(s) Withheld

_____ Trade Secret / Confidential (b4)

__X__ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Administrative #1

If you have any questions, call me at (301) 796-1008.

Sincerely,

{See appended electronic signature page}

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

Attachment

43 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

__X__ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Administrative #2

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/s/

Brian Strongin
10/18/2007 09:58:10 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-056

INFORMATION REQUEST LETTER

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

Dear Mr. Kummeth:

Please refer to your December 20, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec® (omeprazole magnesium) for Delayed-Release Oral Suspension.

We are reviewing the package insert, immediate container, and carton labeling 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.

The following issues/deficiencies have been identified in your proposed labeling.

Package Insert

I. Highlights

A. General Comments

1. You have proposed a Highlights section nearly a full page in length and have requested a waiver of the ½ page requirement for this section.

   The waiver request is under review.

2. A blank space has been included below the statement, "HIGHLIGHTS OF PRESCRIBING INFORMATION.

   This blank space should be deleted.

3. Blank spaces have been included below all section headings.

   These blank spaces should be deleted.

B. The proprietary name, nonproprietary name, and dosage form for Prilosec Delayed-Release Oral Suspension is not listed above the INDICATIONS AND USE section with the listing for Prilosec Capsules.

The proprietary name, nonproprietary name, and dosage form for Prilosec Delayed-Release Oral Suspension should be added following this information for Prilosec capsules.

C. A section for "Recent Major Changes" was not included.

A "Recent Major Changes" section should be added. The full prescribing information (FPI) section title and section number where the changes provided for in NDA 19-810/S-085 (approved April 2007) were added should be listed and the date, "4/07" should be added.

D. The statement, "Revised 11/2006" at the end of the Highlights section should be changed to the month/year the NDA is approved.

Change the statement "Revised 11/2006" at the end of the Highlights section to "Revised 10/2007".

II. Full Prescribing Information: Contents

You have included periods after all section and subsection numbers.

Periods after section and subsection numbers should be deleted.

III. Full Prescribing Information

A. General Comments

1. References are not listed correctly.

The preferred presentation of cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. For example, *[see Use in Specific Populations (8.4)]* not See *Pediatric Use (8.4)*. The cross-reference should be in brackets. Because cross-references are embedded in the text in the FPI, the use of italics to achieve emphasis is encouraged. Do not use all capital letters or bold print.

2. Periods are included after section and subsection numbers

Periods after section and subsection numbers should be deleted.

3. Numbers to one decimal place have been included throughout the label.

Numbers should be rounded to one digit unless they are meaningful at one decimal place.

B. Drug Interaction section

The language provided for in the April 27, 2007 approval letter for NDA 19-810/S-085 was not included in this section.

You should add the language provided in the April 27, 2007 approval letter for NDA 19-810/S-085.

C. How Supplied/Storage and Handling

The manufacturer information, "Manufactured for: AstraZeneca LP, Wilmington, DE 19850" located at the end of this section should be placed after the Patient Counseling Information section.

You should move the statement, "Manufactured for: AstraZeneca LP, Wilmington, DE 19850", to the end of the package insert, after the Patient Counseling Information section.

Carton and Immediate Container Label

1. Please change the established name from "omeprazole" to "omeprazole magnesium".

2. Increase the size and prominence of the established name to ensure that it is ½ the size of the proprietary name.

If you have any questions, call me at (301) 796-2120.

Sincerely,

{See appended electronic signature page}

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

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/s/

Brian Strongin
10/1/2007 10:30:39 AM

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: September 20, 2007

To: George Kummeth	**From:** Brian Strongin, R.Ph., M.B.A.
Company: AstraZeneca LP	Division of Gastroenterology Products
Fax number: (302) 886-2822	**Fax number:**
Phone number: (302) 885-8415	**Phone number:** (301) 796-2120

Subject: Clinical Information Requestg

Total no. of pages including cover: 3

Comments:

Please respond to the attached information request ASAP. Please e-mail the response to me followed by submission of hardcopy. Thanks.

Document to be mailed: ☐ YES ☑ NO

Please provide the following additional data to support the efficacy claims in NDA 22056:

1) Study 251:

The percentage of patients who had the number of vomiting/regurgitation episodes decreased from baseline by 50% (Table 5 and Table 6 of Study 251 submitted to NDA 19,810/S074, Pages 42 and 44; the claims are in the package insert in section 8.4, Pediatric Use, Page 17, NDA 22-056);

2) Study 214:

The study report and data that support the claims "Results showed success rates of 60% (10 mg omeprazole) and 59% (20 mg omeprazole) in reducing the number and intensity of either pain-related symptoms or vomiting/regurgitation episodes." (Submitted to NDA 19,810/S074; the claims are in the package insert in section 8.4, Pediatric Use, Page 17, NDA 22056).

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/s/

Brian Strongin
9/20/2007 08:59:28 AM
CSO

Strongin, Brian K

n: Gallo Torres, Hugo E
: Monday, September 17, 2007 12:38 PM
: Gao, Wen-Yi; Strongin, Brian K
Subject: RE: Re:Clarification: Request of additional data to support the labeling

Brian: Results of Study 214 are already included in the labeling. We should attemp to correct this inaccuracy.

I have spoken to SEALD. This is an opportunity to modify the labeling so that the clinically meaningful message is clear.

In both instances, [251 and 214] we need to express the results as the proportion of patients experiencing response. Referring to the number of episodes of V/R without specifying the proportion of patients experiencing the symptoms is not clinically meaningful.

Thank you.

Hugo

From: Gao, Wen-Yi
Sent: Monday, September 17, 2007 11:48 AM
To: Strongin, Brian K
Cc: Gallo Torres, Hugo E
Subject: Re: Request of additional data to support the labeling

Hi Brian,

As per conversation with Hugo, we need the sponsor to provide the following additional data to support their efficacy claims in NDA 22056:

1) Study 251:
The percentage of patients who had the number of vomiting/regurgitation episodes decreased from the baseline by 50% (Table 5 and Table 6 of Study 251 submitted to NDA 19,810/S074, Pages 42 and 44; The claims are at the Labeling 8.4 Pediatric Use, Page 17, NDA 22056);

2) Study 214:
The study report and data that support the claims "Results showed success rates of 60% (10 mg omeprazole) and 59% (20 mg omeprazole) in reducing the number and intensity of either pain-related symptoms or vomiting/regurgitation episodes." (Submitted to NDA 19,810/S074; The claims are at the Labeling 8.4 Pediatric Use, Page 17, NDA 22056).

Thanks,

Wen-Yi

8/27/07: receipt confirmed

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: August 27, 2007

To: Linda Marino	**From:** Brian Strongin, R.Ph., M.B.A.
Company: AstraZeneca, Inc.	Division of Gastroenterology Products
Fax number: (302) 885-5514	**Fax number:**
Phone number: (302) 885-4442	**Phone number:** (301) 796-2120

Subject: NDA 22-056 Prilosec: Response to Questions in Your August 23, 2007 E-Mail

Total no. of pages including cover: 3

Comments:

Our responses to the questions in your August 23, 2007 E-mail are attached. Thanks.

Document to be mailed: ☐ YES ☑ NO

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/s/

Brian Strongin
8/27/2007 03:30:52 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-056

INFORMATION REQUEST LETTER

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

Dear Mr. Kummeth:

Please refer to your December 20, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec® (omeprazole magnesium) For Delayed-Release Oral Suspension.

We are reviewing the Biophamaceutical 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.

Regarding Study D9586C0002 titled, "A Phase I, Open, Randomized, Three-Way Crossover, Single-Center Biovailability Study Comparing Three Different Formulations of Omeprazole, 20mg Following Single and 5 days Repeated Once Daily Oral Administration in Healthy Male and Female Subjects": please provide the raw data for the freeze-thaw, bench-top, and long-term stability results for omeprazole in the analytical report. In addition, confirm that the stability conditions validated cover the actual analysis conditions.

If you have any questions, call me at (301) 796-1008.

Sincerely,

{See appended electronic signature page}

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

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/s/

Brian Strongin
8/20/2007 12:48:03 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-056

INFORMATION REQUEST LETTER

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

Dear Mr. Kummeth:

Please refer to your December 20, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec (omeprazole magesium) Delayed-Release Oral Suspension.

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.

1. Please provide pharmacokinetic data on the food effects of the omeprazole magnesium sachet formulation. Alternatively, provide your rationale as to why this data is not needed.

2. You state under "5.5.2.3 Drug concentration measurements" that the bioanalytical results are presented in the bioanalytical study validation report 41312-0873 and the method validation is documented in the report PMC-9441. Please provide the locations (page and volume numbers) of these reports in your submission dated December 20, 2006.

If you have any questions, call Ryan Barraco, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Julieann DuBeau, M.S.N, R.N.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Julieann DuBeau
4/23/2007 04:00:29 PM

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 22-056 Supplement # Efficacy Supplement Type

Proprietary Name: Prilosec For Delayed-Release Oral Suspension
Established Name: omeprazole magnesium
Strengths: 20 mg

Applicant: AstraZeneca
Agent for Applicant (if applicable):

Date of Application: December 20, 2006
Date of Receipt: December 20, 2006
Date clock started after UN:
Date of Filing Meeting: February 1, 2007
Filing Date: February 3, 2007
Action Goal Date (optional): User Fee Goal Date: October 20, 2007

Indication(s) requested: For pediatric patients 0-2 years of age:

b(4)

- Treatment of Gastroesophageal Reflux Disease (GERD)
- [redacted] Healing of Erosive Esophagitis

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

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

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

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

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

NOTE: *If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required by contacting the User Fee staff in the Office of Regulatory Policy. The applicant is required to pay a user fee if: (1) the*

product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the User Fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2) application? YES ☐ NO ☒
  If yes, explain:

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

- Does another drug have orphan drug exclusivity for the same indication? YES ☐ NO ☒

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

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

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

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

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

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

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

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

  1. This application is a paper NDA YES ☐

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

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

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

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

Additional comments:

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

Additional comments:

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

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

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

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES ☒ NO ☐

- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES ☐ NO ☐

- Is this submission a partial or complete response to a pediatric Written Request? YES ☐ NO ☒

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES ☒ NO ☐
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: *Financial disclosure is required for bioequivalence studies that are the basis for approval.*

- Field Copy Certification (that it is a true copy of the CMC technical section) YES ☒ NO ☐

- PDUFA and Action Goal dates correct in tracking system? YES ☒ NO ☐
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.

- List referenced IND numbers: b(4)

- Are the trade, established/proper, and applicant names correct in COMIS? YES ☒ NO ☐

If no, have the Document Room make the corrections.

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

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

- Any SPA agreements? Date(s) _____ NO ☒
  If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES ☒ NO ☐
  If no, request in 74-day letter.

- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
  Was the PI submitted in PLR format? YES ☒ NO ☐

  If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:

- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES ☒ NO ☐

- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES ☒ NO ☐

- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?
  N/A ☒ YES ☐ NO ☐

- Risk Management Plan consulted to OSE/IO? N/A ☒ YES ☐ NO ☐

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA ☒ YES ☐ NO ☐

If Rx-to-OTC Switch or OTC application:

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES ☐ NO ☐

- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? YES ☐ NO ☐

Clinical

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

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES ☐ NO ☒
  If no, did applicant submit a complete environmental assessment? YES ☒ NO ☐
  If EA submitted, consulted to EA officer, OPS? YES ☒ NO ☐

- Establishment Evaluation Request (EER) submitted to DMPQ? YES ☐ NO ☐

- If a parenteral product, consulted to Microbiology Team? YES ☐ NO ☐

ATTACHMENT

MEMO OF FILING MEETING

DATE: February 1, 2007

NDA #: 22-056

DRUG NAMES: Prilosec For Delayed-Release Oral Suspension

APPLICANT: AstraZeneca

BACKGROUND: NDA 22-056 was submitted and received on December 20, 2006. This NDA provides for the following indications in pediatric patients —years of age:

b(4)

- Treatment of Gastroesophageal Reflux Disease (GERD)
- —— Healing of Erosive Esophagitis

The NDA was submitted in response to the postmarketing commitment for NDA 19-810/ S-074 which asked the sponsor to develop an age-appropriate formulation of Prilosec in pediatric patients 0-2 years of age. The sponsor was asked to develop a formulation where the enteric coating of the granules remains intact before oral drug administration.

ATTENDEES: Dr. Brian E. Harvey, Director, Division of Gastroenterology (DGP)
Dr. Hugo Gallo-Torres, Team Leader, DGP
Dr. Wen-Yi Gao, Medical Officer, DGP
Dr. Marie Kowblansky, PAL, Division of Pre-marketing Assessment II (DPA II)
Dr. Maria Ysern, Chemistry Reviewer, DPA II
Dr. Jasti Choudary, Supervisory Pharmacologist, DGP
Dr. Sushanta Chakder, Pharmacology Reviewer, DGP
Dr. Milton Fan, Biostatician, Division of Biometrics II
Dr. Tien-Mien Chen, Clinical Pharmacology Reviewer, Division of Clinical Pharmacology III
Mr. Ryan Barraco, Regulatory Project Manager, DGP

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

Discipline/Organization	**Reviewer**
Medical:	Dr. Wen-Yi Gao
Secondary Medical:	
Statistical:	Dr. Milton Fan
Pharmacology:	Dr. Sushanta Chakder
Statistical Pharmacology:	
Chemistry:	Dr. Maria Ysern
Environmental Assessment (if needed):	Dr. Raanan Bloom
Biopharmaceutical:	Dr. Tien-Mien Chen
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	

DSI:
OPS:
Regulatory Project Management: Ryan Barraco
Other Consults:

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

CLINICAL FILE ☒ REFUSE TO FILE ☐

- Clinical site audit(s) needed? YES ☐ NO ☒
  If no, explain:
- Advisory Committee Meeting needed? YES, date if known _____ NO ☒

- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?
  N/A ☒ YES ☐ NO ☐

CLINICAL MICROBIOLOGY N/A ☒ FILE ☐ REFUSE TO FILE ☐

STATISTICS N/A ☐ FILE ☒ REFUSE TO FILE ☐

BIOPHARMACEUTICS FILE ☒ REFUSE TO FILE ☐

- Biopharm. study site audits(s) needed? YES ☒ NO ☐

PHARMACOLOGY/TOX N/A ☐ FILE ☒ REFUSE TO FILE ☐

- GLP audit needed? YES ☐ NO ☒

CHEMISTRY FILE ☒ REFUSE TO FILE ☐

- Establishment(s) ready for inspection? YES ☒ NO ☐
- Sterile product? YES ☐ NO ☐
  If yes, was microbiology consulted for validation of sterilization?
  YES ☐ NO ☐

ELECTRONIC SUBMISSION:
Any comments: N/A

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

☐ The application is unsuitable for filing. Explain why:

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

- ☒ No filing issues have been identified.
- ☐ Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. ☐ Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.

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

3. ☐ If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.

4. ☐ If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)

5. ☐ Convey document filing issues/no filing issues to applicant by Day 74.

Ryan Barraco
Regulatory Project Manager

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/s/

Ryan Barraco
3/12/2007 11:41:37 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-056

INFORMATION REQUEST LETTER

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

Dear Mr. Kummeth:

Please refer to your December 20, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec® (omeprazole magnesium) For Delayed-Release Oral Suspension.

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.

1. Although your study entitled, "A phase I, open, randomized, three-way cross-over, single-centre bioavailability study comparing three different formulations of omeprazole 20 mg following single and 5 days repeated once daily oral administration in healthy male and female subjects" (study number D9586C00002) is a relative bioavailability study, please provide:

    a. The calculations using 90% confidence intervals (CIs) instead of using 95% CIs for the log-transformed pharmacokinetic parameters (i.e., C_{max}, $AUC_{0-\infty}$, and AUC_{0-t}).

    b. Statistical printouts (e.g., estimate, standard error of estimate), according to the Agency's acceptance criteria for bioequivalence assessment. Provide the location or submit SAS Xport data.

2. Please report plasma levels of Prilosec® (omeprazole magnesium) For Delayed-Release Oral Suspension as µg/mL (or ng/mL) instead of µmol/L in Figure 2 (p.43) and PK Tables 9-12 (p.40-41) under Sections 7.1.2 and 7.1.3.

If you have any questions, call Ryan Barraco, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Julieann DuBeau, M.S.N., R.N.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Julieann DuBeau
3/8/2007 04:09:18 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-056

NDA ACKNOWLEDGMENT

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

Dear Mr. Kummeth:

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

Name of Drug Product:	Prilosec® (omeprazole magnesium) For Delayed-Release Oral Suspension
Review Priority Classification:	Standard (S)
Date of Application:	December 20, 2006
Date of Receipt:	December 20, 2006
Our Reference Number:	NDA 22-056

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 18, 2007, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 20, 2007.

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 me at 301-796-0846.

Sincerely,

{See appended electronic signature page}

Ryan Barraco
Regulatory Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Ryan Barraco
2/16/2007 08:53:41 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-056

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

Dear Mr. Kummeth:

Please refer to your December 20, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec® (omeprazole magnesium) For Delayed-Release Oral Suspension.

We also refer to your submission dated February 8, 2007.

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 18, 2007, 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 Ryan Barraco, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Julieann DuBeau, M.S.N., R.N.
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Julieann DuBeau
2/20/2007 02:04:44 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

(Division/Office):
:R OSE CONSULTS
Attention: LCDR Angela Robinson, OSE Regulatory Project Manager
WO22, RM 3435, HFD-430

FROM:
Ryan Barraco, Regulatory Project Manager
Division of Gastroenterology Products
WO22, RM 5109, HFD-180

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
2/20/07		22-056	New NDA	December 20, 2006

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Prilosec® (omeprazole magnesium) For Delayed-Release Oral Suspension	Standard	PPI	September 5, 2007

NAME OF FIRM: AstraZeneca LP

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE–NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☑ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ PE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

The Division of Gastroenterology has receieved a new NDA, Prilosec® (omeprazole magnesium) For Delayed-Release Oral Suspension. We respectfully request that DDMAC and DMETS review the package insert in PLR format, the carton label, and the immediate container label. The NDA is available electronically on the EDR and at the following link: \\CDSESUB1\N22056\N_000\2006-12-20. The PDUFA goal date is October 20, 2007. Please contact me if you have any questions.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Barraco, Regulatory Project Manager	☑ DFS ☐ HAND

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/s/

Ryan Barraco
2/20/2007 01:08:55 PM

DSI CONSULT

Request for Biopharmaceutical Inspections

DATE: February 16, 2007

TO: C.T. Viswanathan, Ph.D.
Associate Director for Bioequivalence
Division of Scientific Investigations, HFD-48

THROUGH: CAPT E. Dennis Bashaw, Pharm.D.
Director, Division of Clinical Pharmacology III (DCP 3)
Office of Clinical Pharmacology

FROM: Ryan Barraco, Regulatory Project Manager, HFD-180

SUBJECT: **Request for Biopharmaceutical Inspections**
NDA 22-056
Prilosec (omeprazole magnesium) Delayed-Release for Oral Suspension 2.5 mg and 10 mg

Study/Site Identification:

The following study and sites pivotal to approval (OR, raise question regarding the quality or integrity of the data submitted and) have been identified for inspection:

Study #	Clinical Site (name, address, phone, fax, contact person, if available)	Analytical Site (name, address, phone, fax, contact person, if available)
D9586C00002	Investigator: Jacob Odenstedt, MD AstraZeneca Clinical Pharmacology Unit Sahlgrenska University Hospital S-413 45 Gothenburg, Sweden	→

b(4)

International Inspections:

(Please note: International inspections require sign-off by the ORM Division Director or DCP Division Director.)

We have requested an international inspection because:

__X__ There is a lack of domestic data that solely supports approval;

_____ Other (please explain):

Goal Date for Completion:

We request that the inspections be conducted and the Inspection Summary Results be provided by **July 20, 2007,** in order for us to meet our regulatory deadlines.

Should you require any additional information, please contact Ryan Barraco at (301) 796-0846.

Concurrence: (Optional)
N/A

CAPT E. Dennis Bashaw, Pharm.D.
Director, Division of Clinical Pharmacology III
Office of Clinical Pharmacology

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/s/

Dennis Bashaw
2/16/2007 01:07:35 PM

ACTION PACKAGE CHECKLIST

Application Information			
BLA # NDA # 22-056	BLA STN# NDA Supplement	If NDA, Efficacy Supplement Type:	
Proprietary Name: Prilosec For Delayed-Release Oral Suspension Established Name: omeprazole magnesium Dosage Form: Oral Suspension		Applicant: AstraZeneca, Inc.	
RPM: Elizabeth A.S. Ford, RN		Division: Division of Gastroenterology Products	Phone # 6-0193

NDAs:	505(b)(2) NDAs and 505(b)(2) NDA supplements:
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.)	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 Date:

❖ User Fee Goal Date ❖ Action Goal Date (if different)	March 14, 2008 March 14, 2008
❖ Actions	
• Proposed action	☒ AP ☐ TA ☐ AE ☐ NA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None Approvable, October 19, 2007
❖ Advertising *(approvals only)* Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed *(indicate dates of reviews)*	☒ Requested in AP letter ☐ Received and reviewed

❖ Application Characteristics

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): 3

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)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

NDAs and NDA Supplements:
☐ OTC drug

Other:

Other comments:

❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP	☐ Yes ☒ No
• 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 ☐ Not an AP action
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Press Office notified of action	☒ Yes ☐ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

❖ Exclusivity	
• NDAs: Exclusivity Summary (approvals only) *(file Summary in* Administrative Documents *section)*	☒ Included
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• 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.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• 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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• 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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• 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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
❖ 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) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☐ 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

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)? ☐ Yes ☐ No

*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? ☐ Yes ☐ No

(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)? ☐ Yes ☐ No

*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? ☐ Yes ☐ No

(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.*	
Summary Reviews	
❖ Summary Reviews (e.g., Office Director, Division Director) *(indicate date for each review)*	October 19, 2007/March 20. 2008
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) *(indicate date)*	
Labeling	
❖ Package Insert	
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	March 20, 2008
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	December 20, 2006
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	X
❖ Patient Package Insert	N/A
• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	
❖ Medication Guide	N/A
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (**full color** carton and immediate-container labels)	
• Most-recent division-proposed labels (only if generated after latest applicant submission)	
• Most recent applicant-proposed labeling	December 13, 2007
❖ Labeling reviews and minutes of any labeling meetings *(indicate dates of reviews and meetings)*	☒ DMETS 5/4/07 ☐ DSRCS ☐ DDMAC ☒ SEALD 10/17/2007 ☒ Other reviews: RPM Review 10/1/07 ☐ Memos of Mtgs

Administrative Documents	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) *(indicate date of each review)*	3/12/07
❖ NDA and NDA supplement approvals only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ AIP-related documents • Center Director's Exception for Review memo • If AP: OC clearance for approval	N/A
❖ Pediatric Page (all actions)	☒ Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. *(Include certification.)*	☒ Verified, statement is acceptable
❖ Postmarketing Commitment Studies	☒ Birth-1year
• Outgoing Agency request for post-marketing commitments *(if located elsewhere in package, state where located)*	Approval letter, T-con 3/20/08
• Incoming submission documenting commitment	
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	X
❖ Internal memoranda, telecons, email, etc.	X
❖ Minutes of Meetings	
• Pre-Approval Safety Conference *(indicate date; approvals only)*	
• Pre-NDA/BLA meeting *(indicate date)*	☒ No mtg
• EOP2 meeting *(indicate date)*	☒ No mtg
• Other (e.g., EOP2a, CMC pilot programs)	N/A
❖ Advisory Committee Meeting	☒ No AC meeting
• Date of Meeting	
• 48-hour alert or minutes, if available	
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A
CMC/Product Quality Information	
❖ CMC/Product review(s) *(indicate date for each review)*	4/6/07; 10/17/07; 2/28/08
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer *(indicate date for each review)*	☒ None
❖ BLAs: Product subject to lot release (APs only)	☐ Yes ☐ No
❖ Environmental Assessment (check one) (original and supplemental applications)	
• ☐ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	
• ☒ Review & FONSI *(indicate date of review)*	3/3/07
• ☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) *(indicate date of each review)*	☒ Not a parenteral product
❖ Facilities Review/Inspection	N/A
❖ NDAs: Facilities inspections (include EER printout)	Date completed: 8/7/07 ☒ Acceptable ☐ Withhold recommendation

❖ 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)*	☐ Requested ☐ Accepted ☐ Hold
❖ NDAs: Methods Validation	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed
Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	8/9/07
❖ 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 carc
❖ ECAC/CAC report/memo of meeting	
❖ Nonclinical inspection review Summary (DSI)	☐ None requested
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	October 17, 2007; February 9, 2008
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	See MO Review Dated October 17, 2007
❖ Clinical consult reviews from other review disciplines/divisions/Centers *(indicate date of each review)*	☒ None
❖ Microbiology (efficacy) reviews(s) *(indicate date of each review)*	☒ Not needed
❖ Safety Update review(s) *(indicate location/date if incorporated into another review)*	Incorporated into 2/9/08 Clinical review.
❖ Risk Management Plan review(s) (including those by OSE) *(indicate location/date if incorporated into another 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	3/13/07; 7/20/07
• Clin Pharm Studies	
❖ Statistical Review(s) *(indicate date for each review)*	☒ None
❖ Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None October 16, 2007

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.