

CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:
22511Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 022511

SUPPL #

HFD #

Trade Name Vimovo

Generic Name naproxen and esomeprazole magnesium delayed release tablets

Applicant Name Pozen

Approval Date, If Known April 30, 2010

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)(2)

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?

No

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#

NDA#

NDA#

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# 020067 | EC Naprosyn |
| NDA# 021153 | Nexium (esomeprazole magnesium) Delayed Release Capsules |
| NDA# 021689 | Nexium IV (esomeprazole sodium) for Injection |
| NDA# 021957 | Nexium (esomeprazole magnesium) for Delayed-Release Oral Suspension |
| NDA# 022101 | Nexium (esomeprazole magnesium) Delayed Release for Oral Suspension |
| NDA# 020204 | Aleve (naproxen sodium) |
| NDA# 021076 | Aleve-D Sinus and Cold (naproxen sodium and pseudoephedrine hydrochloride) |
| NDA# 018164 | Anaprox (naproxen sodium) |
| NDA# 020353 | Naprelan (naproxen sodium) |
| NDA# 017581 | Naprosyn (naproxen sodium) |
| NDA# 018965 | Naprosyn (naproxen sodium) |
| NDA# 021920 | Naproxen Sodium |
| NDA# 021507 | NaprPac 250 mg, 375 mg and 500 mg (lansoprazole and naproxen) |
| NDA# 021926 | Treximet (naproxen sodium and sumatriptan succinate) |

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:

| | | |
|------------------|-----------|---|
| Investigation #1 | PN400-105 | An Open-label, Randomized, Two-Way Crossover Study to Evaluate the Relative Bioavailability of Naproxen Following a Single Oral Dose of PN 400 (375 mg Naproxen/20 mg Esomeprazole) Versus EC-NAPROSYN® 375 mg in Healthy Subjects |
| Investigation #2 | PN400-114 | A Randomized, Open-Label, 4-Way Crossover Study to Evaluate Naproxen and Esomeprazole Plasma Levels in Healthy Subjects Following Oral Administration of PN 400, Enteric-Coated Naproxen 500 MG Plus Enteric-Coated Esomeprazole 20 MG, Enteric-Coated Naproxen 500 MG Alone, and Enteric-Coated Esomeprazole 20 MG Alone |
| Investigation #3 | PN400-301 | A 6-month, Phase 3, Randomized, Double-Blind, Parallel-Group, Controlled, Multi-Center Study to Evaluate the Incidence of Gastric Ulcers Following Administration of Either PN 400 or Naproxen in Subjects who are at Risk for Developing NSAID-Associated Ulcers |
| Investigation #4 | PN400-302 | A 6-month, Phase 3, Randomized, Double-Blind, Parallel-Group, Controlled, Multi-Center Study to Evaluate the Incidence of Gastric Ulcers Following Administration of Either PN 400 or Naproxen in Subjects who are at Risk for Developing NSAID-Associated Ulcers |
| Investigation #5 | PN400-307 | Randomized, Double-Blind, Parallel Group, Placebo-Controlled, Multi-Center Study , Evaluating the Efficacy of PN 400 BID AND Celecoxib 200 MG QD in Patients with Osteoarthritis of the Knee |
| Investigation #6 | PN400-309 | Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Multi-Center Study , Evaluating the Efficacy of PN 400 BID AND Celecoxib 200 MG QD in Patients with Osteoarthritis of the Knee |

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 <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #2 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #3 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #4 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #5 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #6 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |

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 <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #2 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #3 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #4 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #5 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| Investigation #6 | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |

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"):

| | | |
|------------------|-----------|---|
| Investigation #1 | PN400-105 | An Open-label, Randomized, Two-Way Crossover Study to Evaluate the Relative Bioavailability of Naproxen Following a Single Oral Dose of PN 400 (375 mg Naproxen/20 mg Esomeprazole) Versus EC-NAPROSYN® 375 mg in Healthy Subjects |
| Investigation #2 | PN400-114 | A Randomized, Open-Label, 4-Way Crossover Study to Evaluate Naproxen and Esomeprazole Plasma Levels in Healthy Subjects Following Oral Administration of PN 400, Enteric-Coated Naproxen 500 MG Plus Enteric-Coated Esomeprazole 20 MG, Enteric-Coated Naproxen 500 MG Alone, and Enteric-Coated Esomeprazole 20 MG Alone |
| Investigation #3 | PN400-301 | A 6-month, Phase 3, Randomized, Double-Blind, Parallel-Group, Controlled, Multi-Center Study to Evaluate the Incidence of Gastric Ulcers Following Administration of Either PN 400 or Naproxen in Subjects who are at Risk for Developing NSAID-Associated Ulcers |
| Investigation #4 | PN400-302 | A 6-month, Phase 3, Randomized, Double-Blind, Parallel-Group, Controlled, Multi-Center Study to Evaluate the Incidence of Gastric Ulcers Following Administration of Either PN 400 or Naproxen in Subjects who are at Risk for Developing NSAID-Associated Ulcers |
| Investigation #5 | PN400-307 | Randomized, Double-Blind, Parallel Group, Placebo-Controlled, Multi-Center Study , Evaluating the Efficacy of PN 400 BID AND Celecoxib 200 MG QD in Patients with Osteoarthritis of the Knee |
| Investigation #6 | PN400-309 | Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Multi-Center Study , Evaluating the Efficacy of PN 400 BID AND Celecoxib 200 MG QD in Patients with Osteoarthritis of the Knee |

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 # 076301 YES ! NO
! Explain:

Investigation #2
IND # 076301 YES ! NO
! Explain:

Investigation #3
IND # 076301 YES ! NO
! Explain:

Investigation #4
IND # 076301 YES ! NO
! Explain:

Investigation #5
IND # 076301 YES ! NO
! Explain:

Investigation #6
IND # 076301 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: Anna M. Simon
Title: Regulatory Project Manager
Date: 04/30/2010

Name of Office/Division Director signing form: Donna Griebel, M.D.
Title: Director

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

| Application Type/Number | Submission Type/Number | Submitter Name | Product Name |
|-------------------------|------------------------|----------------|--|
| NDA-22511 | ORIG-1 | POZEN INC | PN 400 NAPROXEN/ESOMEPRAZOLE MAGNESIUM |

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

/s/

Anna M SIMON
04/30/2010

DONNA J GRIEBEL
04/30/2010

505(b)(2) ASSESSMENT

| Application Information | | |
|---|----------------------------------|------------------------------|
| NDA # 022511 | NDA Supplement #: S- | Efficacy Supplement Type SE- |
| Proprietary Name: Vimovo Established/Proper Name: naproxen and esomeprazole magnesium Dosage Form: Delayed Release Tablets Strengths: 375 mg naproxen/20 mg esomeprazole and 500 mg naproxen /20 mg esomeprazole | | |
| Applicant: Pozen | | |
| Date of Receipt: June 30, 2009 | | |
| PDUFA Goal Date: April 30, 2010 | Action Goal Date (if different): | |
| Proposed Indication(s): Treatment of the signs and symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis in patients at risk for developing NSAID-associated gastric ulcers. | | |

GENERAL INFORMATION

- 1) Is this application for a recombinant or biologically-derived product and/or protein or peptide product *OR* is the applicant relying on a recombinant or biologically-derived product and/or protein or peptide product to support approval of the proposed product?
YES NO

If "YES" contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

**INFORMATION PROVIDED VIA RELIANCE
(LISTED DRUG OR LITERATURE)**

- 2) List the information essential to the approval of the proposed drug that is provided by reliance on our previous finding of safety and efficacy for a listed drug or by reliance on published literature. *(If not clearly identified by the applicant, this information can usually be derived from annotated labeling.)*

| Source of information* (e.g., published literature, name of referenced product) | Information provided (e.g., pharmacokinetic data, or specific sections of labeling) |
|---|---|
| EC-Naprosyn (NDA 020067, Roche) | Pozen referenced the Agency's previous findings for safety and efficacy for EC-Naprosyn. |
| | |
| | |

*each source of information should be listed on separate rows

- 3) Reliance on information regarding another product (whether a previously approved product or from published literature) must be scientifically appropriate. An applicant needs to provide a scientific "bridge" to demonstrate the relationship of the referenced and proposed products. Describe how the applicant bridged the proposed product to the referenced product(s). (Example: BA/BE studies)

The scientific bridge to demonstrate the relationship of the reference listed drug to the new drug consisted of pharmacokinetic studies that compared the profiles of the naproxen in Vimovo to the currently marketed Naprosyn.

RELIANCE ON PUBLISHED LITERATURE

- 4) (a) Regardless of whether the applicant has explicitly stated a reliance on published literature to support their application, is reliance on published literature necessary to support the approval of the proposed drug product (i.e., the application *cannot* be approved without the published literature)?

YES NO

If "NO," proceed to question #5.

- (b) Does any of the published literature necessary to support approval identify a specific (e.g., brand name) *listed* drug product?

YES NO

If "NO," proceed to question #5.

If "YES", list the listed drug(s) identified by name and answer question #4(c).

- (c) Are the drug product(s) listed in (b) identified by the applicant as the listed drug(s)?

YES NO

RELIANCE ON LISTED DRUG(S)

Reliance on published literature which identifies a specific approved (listed) drug constitutes reliance on that listed drug. Please answer questions #5-9 accordingly.

- 5) Regardless of whether the applicant has explicitly referenced the listed drug(s), does the application **rely** on the finding of safety and effectiveness for one or more listed drugs (approved drugs) to support the approval of the proposed drug product (i.e., the application cannot be approved without this reliance)?

YES NO

If "NO," proceed to question #10.

- 6) Name of listed drug(s) relied upon, and the NDA/ANDA #(s). Please indicate if the applicant explicitly identified the product as being relied upon (see note below):

| Name of Drug | NDA/ANDA # | Did applicant specify reliance on the product? (Y/N) |
|--------------|------------|--|
| EC Naprosyn | NDA 020067 | Y (Form 356h) |
| | | |

Applicants should specify reliance on the 356h, in the cover letter, and/or with their patent certification/statement. If you believe there is reliance on a listed product that has not been explicitly identified as such by the applicant, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

- 7) If this is a (b)(2) supplement to an original (b)(2) application, does the supplement rely upon the same listed drug(s) as the original (b)(2) application?

N/A YES NO

If this application is a (b)(2) supplement to an original (b)(1) application or not a supplemental application, answer "N/A".

If "NO", please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

- 8) Were any of the listed drug(s) relied upon for this application:

- a) Approved in a 505(b)(2) application?

YES NO

If "YES", please list which drug(s).

Name of drug(s) approved in a 505(b)(2) application:

- b) Approved by the DESI process?

YES NO

If "YES", please list which drug(s).

Name of drug(s) approved via the DESI process:

c) Described in a monograph?

YES NO
If "YES", please list which drug(s).

Name of drug(s) described in a monograph:

d) Discontinued from marketing?

YES NO
If "YES", please list which drug(s) and answer question d) i. below.
If "NO", proceed to question #9.

Name of drug(s) discontinued from marketing:

i) Were the products discontinued for reasons related to safety or effectiveness?

YES NO

(Information regarding whether a drug has been discontinued from marketing for reasons of safety or effectiveness may be available in the Orange Book. Refer to section 1.11 for an explanation, and section 6.1 for the list of discontinued drugs. If a determination of the reason for discontinuation has not been published in the Federal Register (and noted in the Orange Book), you will need to research the archive file and/or consult with the review team. Do not rely solely on any statements made by the sponsor.)

9) Describe the change from the listed drug(s) relied upon to support this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsule to solution").

Application NDA 022511 provides for a combination product from the previously approved NDA 020067 and NDA 021153.

The purpose of the following two questions is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.

*The assessment of pharmaceutical equivalence for a recombinant or biologically-derived product and/or protein or peptide product is complex. If you answered **YES to question #1**, proceed to question #12; if you answered **NO to question #1**, proceed to question #10 below.*

10) (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved (via an NDA or ANDA)?

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

Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical equivalent must also be a combination of the same drugs.

YES NO

If "NO" to (a) proceed to question #11.

If "YES" to (a), answer (b) and (c) then proceed to question #12.

(b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval?

YES NO

(c) Is the listed drug(s) referenced by the application a pharmaceutical equivalent?

YES NO

If "YES" to (c) and there are no additional pharmaceutical equivalents listed, proceed to question #12.

If "NO" or if there are additional pharmaceutical equivalents that are not referenced by the application, list the NDA pharmaceutical equivalent(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical equivalent(s):

11) (a) Is there a pharmaceutical alternative(s) already approved (via an NDA or ANDA)?

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

Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical alternative must also be a combination of the same drugs.

YES NO

If "NO", proceed to question #12.

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval?

YES NO

(c) Is the approved pharmaceutical alternative(s) referenced as the listed drug(s)?

YES NO

If "YES" and there are no additional pharmaceutical alternatives listed, proceed to question #12.

If “NO” *or* if there are additional pharmaceutical alternatives that are not referenced by the application, list the NDA pharmaceutical alternative(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical alternative(s):

PATENT CERTIFICATION/STATEMENTS

12) List the patent numbers of all unexpired patents listed in the Orange Book for the listed drug(s) for which our finding of safety and effectiveness is relied upon to support approval of the (b)(2) product.

Listed drug/Patent number(s):

No patents listed *proceed to question #14*

13) Did the applicant address (with an appropriate certification or statement) all of the unexpired patents listed in the Orange Book for the listed drug(s) relied upon to support approval of the (b)(2) product?

YES NO

If “NO”, list which patents (and which listed drugs) were not addressed by the applicant.

Listed drug/Patent number(s):

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

No patent certifications are required (e.g., because application is based solely on published literature that does not cite a specific innovator product)

21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)

21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)

Patent number(s):

21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)

Patent number(s):

Expiry date(s):

21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification). *If Paragraph IV certification*

was submitted, proceed to question #15.

- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the NDA holder/patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above). *If the applicant has a licensing agreement with the NDA holder/patent owner, proceed to question #15.*
- 21 CFR 314.50(i)(1)(ii): No relevant patents.
- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)

Patent number(s):

Method(s) of Use/Code(s):

15) Complete the following checklist **ONLY** for applications containing Paragraph IV certification and/or applications in which the applicant and patent holder have a licensing agreement:

(a) Patent number(s):

(b) Did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified that this b(2) application was filed [21 CFR 314.52(b)]?

YES NO

If "NO", please contact the applicant and request the signed certification.

(c) Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt.

YES NO

If "NO", please contact the applicant and request the documentation.

(d) What is/are the date(s) on the registered mail receipt(s) (i.e., the date(s) the NDA holder and patent owner(s) received notification):

Date(s):

(e) Has the applicant been sued for patent infringement within 45-days of receipt of the notification listed above?

Note that you may need to call the applicant (after 45 days of receipt of the notification) to verify this information **UNLESS** the applicant provided a written statement from the notified patent owner(s) that it consents to an immediate effective date of approval.

YES NO Patent owner(s) consent(s) to an immediate effective date of approval

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22511

ORIG-1

POZEN INC

PN 400
NAPROXEN/ESOMEPRAZOLE
MAGNESIUM

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

/s/

Anna M SIMON
04/30/2010

ACTION PACKAGE CHECKLIST

| APPLICATION INFORMATION ¹ | | |
|---|-------------------------------|---|
| NDA # 022511 BLA # | NDA Supplement # BLA STN # | If NDA, Efficacy Supplement Type: |
| Proprietary Name: Vimovo Established/Proper Name: naproxen and esomeprazole magnesium Dosage Form: Delayed Release Tablets, 375 mg/20 mg and 500 mg/20 mg | | Applicant: Pozen Agent for Applicant (if applicable): |
| RPM: Anna Simon | | Division: DGP |
| <p>NDA: NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(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 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p> | | <p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s): EC-Naprosyn (NDA 020067, Roche)</p> <p>Provide a brief explanation of how this product is different from the listed drug. This is a combination product. <input type="checkbox"/> If no listed drug, check box and explain:</p> <p>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</p> <p>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: 4/30/2010</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p> |
| ❖ Actions | | |
| <ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>April 30, 2010</u> | | <input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR |
| <ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) | | <input checked="" type="checkbox"/> None |
| ❖ If accelerated approval, were promotional materials received? Note: For accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____ | | <input type="checkbox"/> Received |

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

| | |
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| ❖ Application Characteristics ² | |
| <p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p><input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42)</p> <p>Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request</p> <p>Comments:</p> | |
| ❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM (<i>approvals only</i>) | <input type="checkbox"/> Yes, date |
| ❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>) | <input type="checkbox"/> Yes <input type="checkbox"/> No |
| ❖ Public communications (<i>approvals only</i>) | |
| • Office of Executive Programs (OEP) liaison has been notified of action | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| • Press Office notified of action (by OEP) | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |
| • Indicate what types (if any) of information dissemination are anticipated | <input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other |

² Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

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| ❖ Exclusivity | |
| <ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes |
| <ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires: |
| <ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires: |
| <ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires: |
| <ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires: |
| <ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date 10-year limitation expires: |
| ❖ Patent Information (NDAs only) | |
| <ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. | <input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic. |
| <ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. | 21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii) |
| <ul style="list-style-type: none"> [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). | <input checked="" type="checkbox"/> No paragraph III certification Date patent will expire |
| <ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> | <input checked="" type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> 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 notice of certification?

Yes No

(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 the rest of the patent questions.

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).

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| <p>(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?</p> <p>(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).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p> | <input type="checkbox"/> Yes <input type="checkbox"/> No |
|---|--|

CONTENTS OF ACTION PACKAGE

| | |
|---|--|
| ❖ Copy of this Action Package Checklist ³ | 4/30/10 |
| Officer/Employee List | |
| ❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>) | <input checked="" type="checkbox"/> Included |
| Documentation of consent/non-consent by officers/employees | <input checked="" type="checkbox"/> Included |
| Action Letters | |
| ❖ Copies of all action letters (<i>including approval letter with final labeling</i>) | Action(s) and date(s) AP 4/30/10 |
| Labeling | |
| ❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>) | |
| <ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. | 4/29/10 |
| <ul style="list-style-type: none"> • Original applicant-proposed labeling | 6/30/09 |
| <ul style="list-style-type: none"> • Example of class labeling, if applicable | Nexium, NapraPac, EC-Naprosyn |

³ Fill in blanks with dates of reviews, letters, etc.
Version: 12/4/09

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|---|---|
| ❖ Medication Guide/Patient Package Insert/Instructions for Use (<i>write submission/communication date at upper right of first page of each piece</i>) | <input checked="" type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> None |
| <ul style="list-style-type: none"> Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. | 4/29/10 |
| <ul style="list-style-type: none"> Original applicant-proposed labeling | 11/11/09 |
| <ul style="list-style-type: none"> Example of class labeling, if applicable | Treximet |
| ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>) | |
| <ul style="list-style-type: none"> Most-recent draft labeling | 11/11/09 |
| ❖ Proprietary Name <ul style="list-style-type: none"> Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) Review(s) (<i>indicate date(s)</i>) | 9/15/09 4/15/10; 9/10/09 |
| ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) | <input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA 3/19/10 <input checked="" type="checkbox"/> DRISK 4/20/10 <input checked="" type="checkbox"/> DDMAC 3/24/10 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews |
| Administrative / Regulatory Documents | |
| ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) | 3/25/10 |
| ❖ 505(b)(2) Assessment (<i>indicate date</i>) | <input type="checkbox"/> Not a (b)(2) 4/30/10 |
| ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) | <input checked="" type="checkbox"/> Included |
| ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm | |
| <ul style="list-style-type: none"> Applicant in on the AIP | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |
| <ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> If yes, Center Director's Exception for Review memo (<i>indicate date</i>) If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action |
| ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> Date reviewed by PeRC <u>April 14, 2010</u> If PeRC review not necessary, explain: _____ Pediatric Page (<i>approvals only, must be reviewed by PERC before finalized</i>) | <input checked="" type="checkbox"/> 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 (<i>include certification</i>) | <input checked="" type="checkbox"/> Verified, statement is acceptable |
| ❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>) | 3/25/10; 3/16/10; 3/10/10; 3/9/10; 12/16/09; 11/4/09; 10/1/09; 9/11/09; 7/9/09 |
| ❖ Internal memoranda, telecons, etc. | 4/30/10; 4/29/10; 4/22/10; 4/19/10; 3/31/10; 1/8/10; 11/18/09; 10/9/09 |

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 12/4/09

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| ❖ Minutes of Meetings | | |
| • Regulatory Briefing (<i>indicate date of mtg</i>) | | <input checked="" type="checkbox"/> No mtg |
| • If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) | | <input checked="" type="checkbox"/> N/A or no mtg |
| • Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) | | <input type="checkbox"/> No mtg 3/27/09 |
| • EOP2 meeting (<i>indicate date of mtg</i>) | | <input type="checkbox"/> No mtg 7/17/07 |
| • Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>) | | N/A |
| ❖ Advisory Committee Meeting(s) | | <input checked="" type="checkbox"/> No AC meeting |
| • Date(s) of Meeting(s) | | |
| • 48-hour alert or minutes, if available (<i>do not include transcript</i>) | | |
| Decisional and Summary Memos | | |
| ❖ Office Director Decisional Memo (<i>indicate date for each review</i>) | | <input checked="" type="checkbox"/> None |
| Division Director Summary Review (<i>indicate date for each review</i>) | | <input type="checkbox"/> None 4/30/10 |
| Cross-Discipline Team Leader Review (<i>indicate date for each review</i>) | | <input type="checkbox"/> None 4/23/10 |
| PMR/PMC Development Templates (<i>indicate total number</i>) | | <input checked="" type="checkbox"/> None |
| Clinical Information⁵ | | |
| ❖ Clinical Reviews | | |
| • Clinical Team Leader Review(s) (<i>indicate date for each review</i>) | | see CDTL Review |
| • Clinical review(s) (<i>indicate date for each review</i>) | | 4/23/10; 8/20/09 |
| • Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) | | <input checked="" type="checkbox"/> None |
| ❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>) | | See pg 24 of Clinical Review |
| ❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>) | | <input type="checkbox"/> None 4/28/10; 10/1/09; DAARP 2/3/10; PMHS 2/16/10 |
| ❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>) | | <input checked="" type="checkbox"/> Not applicable |
| ❖ Risk Management | | |
| • REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>) | | 11/11/09 |
| • REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) | | 10/9/09 |
| • Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) | | <input checked="" type="checkbox"/> None |
| ❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>) | | <input type="checkbox"/> None requested 3/18/10; 3/17/10; 3/10/10; 7/28/09 |
| Clinical Microbiology | | <input checked="" type="checkbox"/> None |
| ❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>) | | <input type="checkbox"/> None |
| Clinical Microbiology Review(s) (<i>indicate date for each review</i>) | | <input type="checkbox"/> None |
| Biostatistics | | <input type="checkbox"/> None |

⁵ Filing reviews should be filed with the discipline reviews.
Version: 12/4/09

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| ❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> None |
| Statistical Team Leader Review(s) (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> None |
| Statistical Review(s) (<i>indicate date for each review</i>) | <input type="checkbox"/> None 04/19/10; 8/19/09 |
| Clinical Pharmacology <input type="checkbox"/> None | |
| ❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> None |
| Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> None |
| Clinical Pharmacology review(s) (<i>indicate date for each review</i>) | <input type="checkbox"/> None 4/8/10 |
| ❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>) | <input checked="" type="checkbox"/> None |
| Nonclinical <input type="checkbox"/> None | |
| ❖ Pharmacology/Toxicology Discipline Reviews | |
| • ADP/T Review(s) (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> None |
| • Supervisory Review(s) (<i>indicate date for each review</i>) | <input type="checkbox"/> None 04-13-10 |
| • Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>) | <input type="checkbox"/> None 3/17/10; 10/2/09; 8/19/09 |
| ❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> None |
| ❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> No carc |
| ❖ ECAC/CAC report/memo of meeting | <input checked="" type="checkbox"/> None |
| ❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>) | <input checked="" type="checkbox"/> None requested |
| Product Quality <input type="checkbox"/> None | |
| ❖ Product Quality Discipline Reviews | |
| • ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> None |
| • Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>) | <input checked="" type="checkbox"/> None |
| • Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>) | <input type="checkbox"/> None 4/28/10; 4/7/10; 3/9/09 |
| ❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (<i>indicate date of each review</i>) <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) (<i>indicate date of each review</i>) | <input checked="" type="checkbox"/> Not needed |
| ❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>) | <input checked="" type="checkbox"/> None |
| ❖ Environmental Assessment (check one) (original and supplemental applications) | |
| <input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>) | 12/22/09 |
| <input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>) | N/A |
| <input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>) | N/A |

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| ❖ Facilities Review/Inspection | |
| <input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) | Date completed: 3/24/10; 9/4/09; 8/20/09 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation |
| <input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) | Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation |
| ❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>) | <input type="checkbox"/> Completed <input checked="" type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed |

Appendix 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 ADRA.

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22511

ORIG-1

POZEN INC

PN 400
NAPROXEN/ESOMEPRAZOLE
MAGNESIUM

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/s/

Anna M SIMON

05/04/2010



NDA 022511

INFORMATION REQUEST

Pozen
Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vimovo (naproxen/esomeprazole magnesium) Tablets, 375 mg/20 mg and 500 mg/20 mg.

We are in the process of reviewing your labels and labeling contained in the original submission dated June 30, 2009, and we have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

GENERAL COMMENTS FOR LABELS AND LABELING

A. All Labels and Labeling:

1. Revise the dosage form to read “delayed release tablets,” which is the appropriate dosage form for this product as determined by Office of New Drugs Quality Assessment (ONDQA).

B. Container Labels and Carton Labeling:

1. Please amend the presentation of your trade name, established name, and dosage form in all container/closure systems. Separate the dosage form statement from the statement of strength and relocate the dosage form statement (i.e., delayed release tablets) directly beneath the established name, which is the customary position for the dosage form statement. In addition, increase the prominence of the dosage form statement commensurate with the presentation of the established name. Provide the equivalency statement for both strengths on the container/closures as follows:

Vimovo
(naproxen and esomeprazole magnesium)
delayed release tablets

375 mg/20 mg*

**Each tablet contains 22.3 mg esomeprazole magnesium, equivalent to 20 mg esomeprazole.*

Vimovo
(naproxen and esomeprazole magnesium)
delayed release tablets

500 mg/20 mg*

**Each tablet contains 22.3 mg esomeprazole magnesium, equivalent to 20 mg esomeprazole.*

2. Provide the NDC # on both bottles and blister primary and secondary container/closure labels.
3. The current font utilized for the established name causes the letters to appear too close together and, consequently, difficult to read. Revise the font to a more readable presentation.
4. Remove (b) (4) from the strength panel (375 mg/20 mg (b) (4) -or 500 mg/20 mg (b) (4)).
5. Increase the prominence of the “Dispense with Enclosed Medication Guide” statement and relocate the statement to the principle display panel. 21 C.F.R. §208.24(d) states that this statement “shall appear on the [container] label in a prominent and conspicuous manner.” The ‘conspicuous’ requirement is customarily achieved by placement of the statement on the principle display panel.
6. Add a statement to the side panel consistent with the statement located in the package insert that instructs that “*Vimovo should be swallowed whole and should be taken at least 30 minutes before meals.*” This statement communicates information important to patients that this Naproxen-containing medication is administered differently than other Naproxen products that patients may be accustomed to taking with food. Given that this product will be available as a 6-count professional sample and 60-count unit of use bottle, patients may receive their prescriptions in the manufacturer’s container and have the opportunity to see the statement as a reminder with each dose.
7. Please provide the color mock ups of the container/closures with indicated changes.

C. Container Labels:

1. Remove the Relocate the “*Manufactured for. . . By. . .*” statement away from the principle display panel. This non-critical information crowds the principle display panel.
2. Relocate the “Each tablet contains...” statement to the side panel to provide room for revisions to the label as noted in B-1 through B-4.

If you have any questions, call Anna Simon, Regulatory Project Manager, at 301-796-3509.

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

| Application Type/Number | Submission Type/Number | Submitter Name | Product Name |
|----------------------------|---------------------------|----------------|--|
| NDA-22511 | ORIG-1 | POZEN INC | PN 400 NAPROXEN/ESOMEPRAZOLE MAGNESIUM |

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/s/

Anna M SIMON
03/16/2010

BRIAN K STRONGIN
03/16/2010



NDA 022511

INFORMATION REQUEST

Pozen
Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vimovo (naproxen/esomeprazole magnesium) Tablets, 375 mg/20 mg and 500 mg/20 mg.

(b) (4)

We have the following comments and information requests. In order to facilitate a timely review of your NDA, please provide written response by March 22, 2010. While discussion and agreement on waivers and deferrals should occur during the drug development process, they do not become final until the time of product approval. Additionally, requests for waivers and deferrals, along with the corresponding pediatric plan(s) must be reviewed by the Pediatric Review Committee (PeRC) prior to approval of the NDA.

- Under the criteria established by law, we have determined that a full waiver is reasonable for the indications listed in #1 and #2 below. A full waiver cannot be supported for the indication listed in #3. Thus, as specified below, you must submit additional information.
 1. For the indication, relief of signs and symptoms of **osteoarthritis** (OA) and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers, your request for a full waiver appears reasonable because studies would be impossible or highly impracticable.
 2. For the indication, relief of signs and symptoms of **ankylosing spondylitis** (AS) and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers, your request for a full waiver appears reasonable because studies would be impossible or highly impracticable.
 3. For the indication, relief of signs and symptoms of **rheumatoid arthritis** (RA) and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers, a partial waiver for patients under 2 years of age appears reasonable because studies would be highly impracticable. We therefore recommend you submit a partial waiver request for patients less than 2 years of age, with data to support your request. However, for patients 2 years of age through 16 years 11 months, you must submit a deferral request. Accompany this deferral request with certification of the grounds for deferring the assessments, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a pediatric plan. The plan must include a description of studies needed to support dosing, safety and efficacy in the pediatric population and timelines to include the following dates (month, day year):
 - Protocol Submission
 - Study Completion
 - Final Report Submission

There is a possibility that the efficacy of PN400 for the deferred indication may be extrapolated from adults requiring the relief of signs and symptoms of rheumatoid arthritis and/or decreasing the risk of developing gastric ulcers. Extrapolation of efficacy requires data to support the conclusion that the course of the disease and the effect of treatment are reasonably similar in pediatric and adult patients. We request that you provide data to support that the course of the disease and the effect of treatment are reasonably similar in pediatric and adult patients for the deferred indication (the relief of signs and symptoms of rheumatoid arthritis and decreasing the risk of developing gastric ulcers), if you believe that this conclusion is supported by the data. Please note that even if extrapolation of efficacy is possible, studies to support dosing and safety of this product in the pediatric population from 2 years through 16 years 11 months will be required.

If you have any questions, call Anna Simon, Regulatory Project Manager at (301) 796-3509.

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

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22511

GI-1

POZEN INC

PN 400
NAPROXEN/ESOMEPRAZOLE
MAGNESIUM

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/s/

BRIAN K STRONGIN

03/10/2010



NDA 022511

INFORMATION REQUEST

Pozen
Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vimovo (naproxen/esomeprazole magnesium) Tablets, 375 mg/20 mg and 500 mg/20 mg.

We are reviewing the Clinical 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. We have attempted to reproduce the Adverse Event (AE) incidence table. AE incidence tables were created for trials PN400-301 and PN400-302 individually and then combined using the ADAE analysis dataset. The third most frequently reported preferred term is missing for all three analyses. Please provide additional information on this. A copy of the AE incidence tables is attached for your review.

If you have any questions, call Anna Simon, Regulatory Project Manager, at 301-796-3509.

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

AE Incidence table 301

| | P_TERM | N Rows | N(NAPROXEN) | N(PN400) |
|----|------------------------------------|--------|-------------|----------|
| 1 | Gastritis erosive | 126 | 81 | 45 |
| 2 | Dyspepsia | 101 | 65 | 36 |
| 3 | | 92 | 44 | 48 |
| 4 | Gastritis | 67 | 28 | 39 |
| 5 | Erosive duodenitis | 34 | 30 | 4 |
| 6 | Abdominal pain upper | 27 | 18 | 9 |
| 7 | Diarrhoea | 27 | 13 | 14 |
| 8 | Oesophagitis | 24 | 17 | 7 |
| 9 | Duodenitis | 23 | 19 | 4 |
| 10 | Hiatus hernia | 22 | 14 | 8 |
| 11 | Abdominal distension | 21 | 10 | 11 |
| 12 | Nausea | 20 | 11 | 9 |
| 13 | Flatulence | 18 | 9 | 9 |
| 14 | Upper respiratory tract infection | 13 | 8 | 5 |
| 15 | Cough | 12 | 6 | 6 |
| 16 | Erosive oesophagitis | 12 | 12 | 0 |
| 17 | Constipation | 11 | 7 | 4 |
| 18 | Bronchitis | 10 | 4 | 6 |
| 19 | Nasopharyngitis | 10 | 8 | 2 |
| 20 | Abdominal discomfort | 9 | 6 | 3 |
| 21 | Abdominal pain | 9 | 5 | 4 |
| 22 | Abdominal pain lower | 9 | 4 | 5 |
| 23 | Gastrooesophageal reflux disease | 8 | 7 | 1 |
| 24 | Headache | 8 | 2 | 6 |
| 25 | Gastritis haemorrhagic | 7 | 3 | 4 |
| 26 | Influenza | 7 | 3 | 4 |
| 27 | Urinary tract infection | 7 | 1 | 6 |
| 28 | Anaemia | 6 | 2 | 4 |
| 29 | Dysgeusia | 6 | 2 | 4 |
| 30 | Eructation | 6 | 2 | 4 |
| 31 | Muscle spasms | 6 | 0 | 6 |
| 32 | Pharyngolaryngeal pain | 6 | 4 | 2 |
| 33 | Sinusitis | 6 | 3 | 3 |
| 34 | Vomiting | 6 | 3 | 3 |
| 35 | Arthralgia | 5 | 2 | 3 |
| 36 | Dizziness | 5 | 2 | 3 |
| 37 | Hypertension | 5 | 3 | 2 |
| 38 | Osteoarthritis | 5 | 2 | 3 |
| 39 | Sinus congestion | 5 | 4 | 1 |
| 40 | Breath odour | 4 | 2 | 2 |
| 41 | Contusion | 4 | 1 | 3 |
| 42 | Dermatitis contact | 4 | 2 | 2 |
| 43 | Fatigue | 4 | 3 | 1 |
| 44 | Localised infection | 4 | 2 | 2 |
| 45 | Oedema peripheral | 4 | 2 | 2 |
| 46 | Rash | 4 | 0 | 4 |
| 47 | Acquired oesophageal web | 3 | 1 | 2 |
| 48 | Back pain | 3 | 2 | 1 |
| 49 | Dyspnoea | 3 | 2 | 1 |
| 50 | Gastric polyps | 3 | 1 | 2 |
| 51 | Gastrointestinal mucosal disorder | 3 | 2 | 1 |
| 52 | Haemorrhoids | 3 | 2 | 1 |
| 53 | Musculoskeletal pain | 3 | 0 | 3 |
| 54 | Non-cardiac chest pain | 3 | 1 | 2 |
| 55 | Oesophageal stenosis | 3 | 2 | 1 |
| 56 | Tooth abscess | 3 | 0 | 3 |
| 57 | Type 2 diabetes mellitus | 3 | 1 | 2 |
| 58 | Abdominal tenderness | 2 | 2 | 0 |
| 59 | Alanine aminotransferase increased | 2 | 1 | 1 |
| 60 | Arthritis | 2 | 2 | 0 |
| 61 | Balance disorder | 2 | 1 | 1 |
| 62 | Barrett's oesophagus | 2 | 1 | 1 |
| 63 | Cardiomegaly | 2 | 0 | 2 |
| 64 | Depression | 2 | 1 | 1 |
| 65 | Dry mouth | 2 | 0 | 2 |
| 66 | Frequent bowel movements | 2 | 0 | 2 |
| 67 | Fungal infection | 2 | 0 | 2 |
| 68 | Hepatic enzyme increased | 2 | 1 | 1 |
| 69 | Hypoesthesia | 2 | 1 | 1 |
| 70 | Meniscus lesion | 2 | 2 | 0 |
| 71 | Neck pain | 2 | 2 | 0 |
| 72 | Oesophageal haemorrhage | 2 | 2 | 0 |

AE Incidence for 302

| | P_TERM | N Rows | N(NAPROXEN) | N(PN400) |
|----|---------------------------------------|--------|-------------|----------|
| 1 | Gastritis erosive | 119 | 81 | 38 |
| 2 | Dyspepsia | 90 | 49 | 41 |
| 3 | | 89 | 37 | 52 |
| 4 | Gastritis | 66 | 32 | 34 |
| 5 | Abdominal pain upper | 34 | 19 | 15 |
| 6 | Erosive duodenitis | 25 | 20 | 5 |
| 7 | Upper respiratory tract infection | 24 | 8 | 16 |
| 8 | Nausea | 23 | 10 | 13 |
| 9 | Oesophagitis | 23 | 15 | 8 |
| 10 | Diarrhoea | 21 | 9 | 12 |
| 11 | Hiatus hernia | 21 | 11 | 10 |
| 12 | Duodenitis | 14 | 12 | 2 |
| 13 | Erosive oesophagitis | 14 | 12 | 2 |
| 14 | Constipation | 12 | 5 | 7 |
| 15 | Abdominal distension | 11 | 6 | 5 |
| 16 | Abdominal pain lower | 11 | 7 | 4 |
| 17 | Flatulence | 11 | 4 | 7 |
| 18 | Gastrooesophageal reflux disease | 11 | 8 | 3 |
| 19 | Sinusitis | 11 | 6 | 5 |
| 20 | Arthralgia | 10 | 8 | 2 |
| 21 | Cough | 9 | 5 | 4 |
| 22 | Dysgeusia | 9 | 4 | 5 |
| 23 | Headache | 9 | 4 | 5 |
| 24 | Urinary tract infection | 9 | 5 | 4 |
| 25 | Abdominal pain | 8 | 2 | 6 |
| 26 | Back pain | 8 | 3 | 5 |
| 27 | Bronchitis | 8 | 4 | 4 |
| 28 | Gastritis haemorrhagic | 7 | 6 | 1 |
| 29 | Hypertension | 7 | 4 | 3 |
| 30 | Breath odour | 6 | 3 | 3 |
| 31 | Musculoskeletal pain | 6 | 3 | 3 |
| 32 | Gastroenteritis viral | 5 | 3 | 2 |
| 33 | Haemorrhoids | 5 | 2 | 3 |
| 34 | Rash | 5 | 2 | 3 |
| 35 | Reflux oesophagitis | 5 | 3 | 2 |
| 36 | Tension headache | 5 | 4 | 1 |
| 37 | Abdominal discomfort | 4 | 2 | 2 |
| 38 | Anaemia | 4 | 2 | 2 |
| 39 | Barrett's oesophagus | 4 | 2 | 2 |
| 40 | Nasopharyngitis | 4 | 2 | 2 |
| 41 | Neck pain | 4 | 2 | 2 |
| 42 | Oedema peripheral | 4 | 2 | 2 |
| 43 | Osteoarthritis | 4 | 2 | 2 |
| 44 | Stomach discomfort | 4 | 3 | 1 |
| 45 | Vomiting | 4 | 3 | 1 |
| 46 | Blood urea increased | 3 | 3 | 0 |
| 47 | Cholelithiasis | 3 | 2 | 1 |
| 48 | Depression | 3 | 1 | 2 |
| 49 | Dizziness | 3 | 2 | 1 |
| 50 | Eructation | 3 | 3 | 0 |
| 51 | Gastric polyps | 3 | 0 | 3 |
| 52 | Irritable bowel syndrome | 3 | 2 | 1 |
| 53 | Muscle spasms | 3 | 1 | 2 |
| 54 | Nephrolithiasis | 3 | 1 | 2 |
| 55 | Pneumonia | 3 | 3 | 0 |
| 56 | Upper limb fracture | 3 | 2 | 1 |
| 57 | Abdominal tenderness | 2 | 2 | 0 |
| 58 | Acquired oesophageal web | 2 | 1 | 1 |
| 59 | Arthritis | 2 | 1 | 1 |
| 60 | Blood creatinine increased | 2 | 2 | 0 |
| 61 | Bronchospasm | 2 | 0 | 2 |
| 62 | Chronic obstructive pulmonary disease | 2 | 1 | 1 |
| 63 | Contusion | 2 | 1 | 1 |
| 64 | Duodenitis haemorrhagic | 2 | 1 | 1 |
| 65 | Gastric haemorrhage | 2 | 2 | 0 |
| 66 | Gastroenteritis | 2 | 0 | 2 |
| 67 | Gastroenteritis bacterial | 2 | 2 | 0 |
| 68 | Influenza | 2 | 2 | 0 |
| 69 | Joint injury | 2 | 0 | 2 |
| 70 | Liver function test abnormal | 2 | 1 | 1 |
| 71 | Meniscus lesion | 2 | 1 | 1 |
| 72 | Nodule | 2 | 1 | 1 |

| | P_TERM | N Rows | N(NAPROXEN) | N(PN400) |
|----|------------------------------------|--------|-------------|----------|
| 1 | Gastritis erosive | 245 | 162 | 83 |
| 2 | Dyspepsia | 191 | 114 | 77 |
| 3 | | 181 | 81 | 100 |
| 4 | Gastritis | 133 | 60 | 73 |
| 5 | Abdominal pain upper | 61 | 37 | 24 |
| 6 | Erosive duodenitis | 59 | 50 | 9 |
| 7 | Diarrhoea | 48 | 22 | 26 |
| 8 | Oesophagitis | 47 | 32 | 15 |
| 9 | Hiatus hernia | 43 | 25 | 18 |
| 10 | Nausea | 43 | 21 | 22 |
| 11 | Duodenitis | 37 | 31 | 6 |
| 12 | Upper respiratory tract infection | 37 | 16 | 21 |
| 13 | Abdominal distension | 32 | 16 | 16 |
| 14 | Flatulence | 29 | 13 | 16 |
| 15 | Erosive oesophagitis | 26 | 24 | 2 |
| 16 | Constipation | 23 | 12 | 11 |
| 17 | Cough | 21 | 11 | 10 |
| 18 | Abdominal pain lower | 20 | 11 | 9 |
| 19 | Gastrooesophageal reflux disease | 19 | 15 | 4 |
| 20 | Bronchitis | 18 | 8 | 10 |
| 21 | Abdominal pain | 17 | 7 | 10 |
| 22 | Headache | 17 | 6 | 11 |
| 23 | Sinusitis | 17 | 9 | 8 |
| 24 | Urinary tract infection | 16 | 6 | 10 |
| 25 | Arthralgia | 15 | 10 | 5 |
| 26 | Dysgeusia | 15 | 6 | 9 |
| 27 | Gastritis haemorrhagic | 14 | 9 | 5 |
| 28 | Nasopharyngitis | 14 | 10 | 4 |
| 29 | Abdominal discomfort | 13 | 8 | 5 |
| 30 | Hypertension | 12 | 7 | 5 |
| 31 | Back pain | 11 | 5 | 6 |
| 32 | Anaemia | 10 | 4 | 6 |
| 33 | Breath odour | 10 | 5 | 5 |
| 34 | Vomiting | 10 | 6 | 4 |
| 35 | Eruclation | 9 | 5 | 4 |
| 36 | Influenza | 9 | 5 | 4 |
| 37 | Muscle spasms | 9 | 1 | 8 |
| 38 | Musculoskeletal pain | 9 | 3 | 6 |
| 39 | Osteoarthritis | 9 | 4 | 5 |
| 40 | Rash | 9 | 2 | 7 |
| 41 | Dizziness | 8 | 4 | 4 |
| 42 | Haemorrhoids | 8 | 4 | 4 |
| 43 | Oedema peripheral | 8 | 4 | 4 |
| 44 | Pharyngolaryngeal pain | 7 | 5 | 2 |
| 45 | Reflux oesophagitis | 7 | 3 | 4 |
| 46 | Sinus congestion | 7 | 5 | 2 |
| 47 | Barrett's oesophagus | 6 | 3 | 3 |
| 48 | Contusion | 6 | 2 | 4 |
| 49 | Gastric polyps | 6 | 1 | 5 |
| 50 | Gastroenteritis viral | 6 | 3 | 3 |
| 51 | Neck pain | 6 | 4 | 2 |
| 52 | Acquired oesophageal web | 5 | 2 | 3 |
| 53 | Depression | 5 | 2 | 3 |
| 54 | Dermatitis contact | 5 | 2 | 3 |
| 55 | Fatigue | 5 | 4 | 1 |
| 56 | Non-cardiac chest pain | 5 | 2 | 3 |
| 57 | Stomach discomfort | 5 | 4 | 1 |
| 58 | Tension headache | 5 | 4 | 1 |
| 59 | Tooth abscess | 5 | 1 | 4 |
| 60 | Abdominal tenderness | 4 | 4 | 0 |
| 61 | Arthritis | 4 | 3 | 1 |
| 62 | Dyspnoea | 4 | 2 | 2 |
| 63 | Localised infection | 4 | 2 | 2 |
| 64 | Meniscus lesion | 4 | 3 | 1 |
| 65 | Nephrolithiasis | 4 | 1 | 3 |
| 66 | Oesophageal stenosis | 4 | 3 | 1 |
| 67 | Oesophageal ulcer | 4 | 3 | 1 |
| 68 | Palpitations | 4 | 2 | 2 |
| 69 | Pneumonia | 4 | 4 | 0 |
| 70 | Alanine aminotransferase increased | 3 | 1 | 2 |
| 71 | Blood creatinine increased | 3 | 2 | 1 |
| 72 | Blood urea increased | 3 | 3 | 0 |

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22511

ORIG-1

POZEN INC

PN 400
NAPROXEN/ESOMEPRAZOLE
MAGNESIUM

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/s/

BRIAN K STRONGIN

03/09/2010



NDA 022511

INFORMATION REQUEST

Pozen
Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vimovo (naproxen/esomeprazole magnesium) Tablets, 375 mg/20 mg and 500 mg/20 mg.

We are reviewing the Clinical 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. In the analysis using the "ITT without LOCF", how was the analysis population defined? Were they completers? If yes, the number of subjects in the "ITT/without LOCF" analysis is inconsistent with the number of completers, for example, in Study 307 n=187 for PN400 from the ITT/without LOCF but n=208 completers in your Table 4.
2. In contrast to the ITT/LOCF analysis, the PP/LOCF analysis in Study 307 failed to show superiority of both PN400 and celecoxib over placebo for WOMAC Pain and Function. Please explain.

If you have any questions, call Anna Simon, Regulatory Project Manager at (301) 796-3509.

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

Application
Type/Number

Submission
Type/Number

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Product Name

NDA-22511

ORIG-1

POZEN INC

PN 400
NAPROXEN/ESOMEPRAZOLE
MAGNESIUM

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/s/

BRIAN K STRONGIN

12/16/2009



NDA 22-511

INFORMATION REQUEST

Pozen, Inc.
Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, NC 27517

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PN 400 (naproxen, 500 mg or 375 mg, and esomeprazole magnesium, 20 mg) Tablets.

We also refer to your June 30, 2009, submission, containing the Environmental Assessment for Naproxen and Esomeprazole.

We are reviewing the Environmental Analysis (EA) 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.

We note that this NDA is for a combination product of two previously approved drugs. If the indications, dosage and duration of use for the combination is the same as for the individual drugs previously approved, this NDA would qualify for categorical exclusion under 21 CFR 25.31(a). See Attachment A of the CDER Environmental Assessment Guidance Document.

Under such qualification, we request that you submit a claim for exclusion for each of the previously approved products contained in your combination product, naproxen and esomeprazole magnesium. Information on how to request a categorical exclusion is available at <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm088977.htm>.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Anna Maria Simon, Regulatory Project Manager the Office of New Drugs (AnnaMaria.Simon@fda.hhs.gov).

If you have any questions regarding this letter, call Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

| Application Type/Number | Submission Type/Number | Submitter Name | Product Name |
|-------------------------|------------------------|----------------|--|
| NDA-22511 | ORIG-1 | POZEN INC | PN 400 NAPROXEN/ESOMEPRAZOLE MAGNESIUM |

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/s/

MOO JHONG RHEE
11/04/2009
Chief, Branch III



NDA 022511

INFORMATION REQUEST

Pozen

Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Vimovo (naproxen/esomeprazole magnesium) Tablets, 375 mg/20 mg and 500 mg/20 mg.

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

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)).

In accordance with section 505-1 of the FDCA, we have determined that a REMS is necessary for Vimovo (naproxen/esomeprazole magnesium) to ensure that the benefits of the drug outweigh the risks of cardiovascular and gastrointestinal adverse events.

Your proposed REMS must include the following:

Medication Guide: As one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Vimovo (naproxen/esomeprazole magnesium) poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Vimovo (naproxen/esomeprazole magnesium). FDA has determined that Vimovo (naproxen/esomeprazole magnesium) has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use, Vimovo (naproxen/esomeprazole magnesium).

Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Vimovo (naproxen/esomeprazole magnesium).

Timetable for Submission of Assessments: The proposed REMS must include a timetable for submission of assessments that shall be no less frequent than by 18 months, 3 years, and in the 7th year after the REMS is initially approved. You should specify the reporting interval (dates) that each assessment will cover and the planned date of submission to the FDA of the assessment. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. For example, the reporting interval covered by an assessment that is to be submitted by July 31st should conclude no earlier than June 1st.

Your proposed REMS submission should include two parts: a “proposed REMS” and a “REMS supporting document.” Attached is a template for the proposed REMS that you should complete with concise, specific information (see Appendix A). Once FDA finds the content of the REMS acceptable and determines that the application can be approved, we will include this document and the Medication Guide as attachments to the approval letter that includes the REMS. The REMS, once approved, will create enforceable obligations.

The REMS supporting document should be a document explaining the rationale for each of the elements included in the proposed REMS (see Appendix B).

Your assessment of the REMS should include:

- a. An evaluation of patients’ understanding of the serious risks of Vimovo (naproxen/esomeprazole magnesium).
- b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
- c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

Before we can continue our evaluation of this NDA, you will need to submit the proposed REMS.

Under 21 CFR 208.24(d), you are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided. You should submit marked up carton and container labels of all strengths and formulations with the required statement alerting the dispenser to provide the Medication Guide. We recommend the following language dependent upon whether the Medication Guide accompanies the product or is enclosed in the carton (for example, unit of use):

- “Dispense the enclosed Medication Guide to each patient.” or
- “Dispense the accompanying Medication Guide to each patient.”

Prominently identify the proposed REMS submission with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 022511
PROPOSED REMS**

Prominently identify subsequent submissions related to the proposed REMS with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 022511
PROPOSED REMS-AMENDMENT**

If you do not submit electronically, please send 5 copies of your REMS-related submissions.

If you have any questions, call Anna Simon, Regulatory Project Manager, at (301) 796-3509.

Sincerely,

{See appended electronic signature page}

Donna Griebel, M.D.
Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosures:

Appendix A – REMS Template

Appendix B – REMS Supporting Document Template

APPENDIX A: MEDICATION GUIDE REMS TEMPLATE

Application number TRADE NAME (DRUG NAME)

Class of Product as per label

Applicant name

Address

Contact Information

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

List the goals and objectives of the REMS.

II. REMS ELEMENTS:

A. Medication Guide

If a Medication Guide is included in the proposed REMS, include the following:

A Medication Guide will be dispensed with each [drug name] prescription. [Describe in detail how you will comply with 21 CFR 208.24.]

B. Timetable for Submission of Assessments

For products approved under an NDA or BLA, specify the timetable for submission of assessments of the REMS. The timetable for submission of assessments shall be no less frequent than by 18 months, 3 years, and in the 7th year after the REMS is initially approved. You should specify the reporting interval (dates) that each assessment will cover and the planned date of submission to the FDA of the assessment. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. For example, the reporting interval covered by an assessment that is to be submitted by July 31st should conclude no earlier than June 1st.

APPENDIX B:

REMS SUPPORTING DOCUMENT TEMPLATE

MEDICATION GUIDE REMS

This REMS Supporting Document should include the following listed sections 1 through 6. Include in section 4 the reason that the Medication Guide proposed to be included in the REMS is necessary to ensure that the benefits of the drug outweigh the risks.

1. Table of Contents
2. Background
3. Goals
4. Supporting Information on Proposed REMS Elements
 - a. Medication Guide
 - b. Timetable for Submission of Assessments of the REMS (for products approved under an NDA or BLA)
5. REMS Assessment Plan (for products approved under an NDA or BLA)
6. Other Relevant Information

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22511

ORIG-1

POZEN INC

PN 400
NAPROXEN/ESOMEPRAZOLE
MAGNESIUM

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/s/

DONNA J GRIEBEL

10/09/2009



NDA 022511

INFORMATION REQUEST

Pozen

Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vimovo (naproxen/esomeprazole magnesium) Tablets, 375 mg/20 mg and 500 mg/20 mg.

We are reviewing the Biopharmaceutics 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.

(b) (4)

If you have any questions, call Anna Simon, Regulatory Project Manager at (301) 796-3509.

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

Application
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/s/

BRIAN K STRONGIN

10/01/2009



NDA 22511

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

POZEN Inc.
1414 Raleigh Road, Suite 400
Chapel Hill, NC 27517

ATTENTION: Paul A. Ossi
Senior Vice President, Regulatory Affairs

Dear Mr. Ossi:

Please refer to your New Drug Application (NDA) dated June 30, 2009, received June 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Naproxen and Eesomeprazole Magnesium Tablets, 375 mg/20 mg and 500 mg/20 mg.

We also refer to your June 30, 2009, correspondence, received June 30, 2009, requesting review of your proposed proprietary name, Vimovo. We have completed our review of the proposed proprietary name, Vimovo and have concluded that it is acceptable.

The proposed proprietary name, Vimovo, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your June 30, 2009 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Nina Ton, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-1648. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Chantal Phillips at 301-796-2259.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22511

ORIG-1

POZEN INC

PN 400
NAPROXEN/ESOMEPRAZOLE
MAGNESIUM

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/s/

CAROL A HOLQUIST

09/15/2009



NDA 22-511

FILING COMMUNICATION

Pozen
Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

Please refer to your new drug application (NDA) dated June 30, 2009, received June 30, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (naproxen/esomeprazole magnesium) Tablets, 375 mg/20 mg and 500 mg/20 mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Standard**. Therefore, the user fee goal date is April 30, 2010.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by March 15, 2010.

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

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the

product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Anna Simon, Regulatory Project Manager, at (301) 796-3509.

Sincerely,

{See appended electronic signature page}

Donna Griebel, M.D.
Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22511

ORIG-1

POZEN INC

PN 400
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MAGNESIUM

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/s/

DONNA J GRIEBEL

09/11/2009



NDA 22-511

NDA ACKNOWLEDGMENT

Pozen
Attention: Paul A. Ossi
Senior Vice President, Regulatory Affairs
1414 Raleigh Road
Suite 400
Chapel Hill, N.C. 27517

Dear Mr. Ossi:

We have received your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: (naproxen/esomeprazole magnesium) Tablets, 375 mg/20 mg and 500 mg/20 mg

Date of Application: June 30, 2009

Date of Receipt: June 30, 2009

Our Reference Number: NDA 22-511

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 August 28, 2009 in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

The NDA number provided above should be cited 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

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

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

Sincerely,

{See appended electronic signature page}

Chantal Phillips, M.S.H.S.
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Chantal N. Phillips
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