IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Brian Ault, *et al*.	Filed: September 3, 2009
Application No: 12/553,107	Attorney Docket No: 103526-US/NS
Examiner: Gina C. Yu	Confirmation No. 5949
Title: Method for Delivering a Pharmaceutical Composition to Patient in Need Thereof	

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Commissioner for Patents
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AMENDMENT B IN RESPONSE TO JANUARY 5, 2012 OFFICE ACTION

This amendment is being filed in response to the January 5, 2012 Office action in the above-referenced patent application.

Claim amendments: begin on page **2**.

Remarks begin on page **5**.

Claim Amendments

Please amend the claims as follows:

Claims 1-18 (cancelled).

19. (**currently amended**) A method for ~~**delivering a pharmaceutical composition to a patient in need thereof, comprising:**~~ **treating osteoarthritis, rheumatoid arthritis, or ankylosing spondylitis comprising orally** administering to ~~**said**~~ **a** patient ~~**a pharmaceutical composition**~~ in **need thereof an AM** unit dose form ~~**comprising**~~ **and, 10 hours (±20%) later, a PM unit dose form, wherein:**

the AM and PM unit dose forms each comprises:

naproxen, or a pharmaceutically acceptable salt thereof, **in an amount to provide 500 mg of naproxen,** and

esomeprazole, or a pharmaceutically acceptable salt thereof, **in an amount to provide 20 mg of esomeprazole**;

~~**wherein**~~

said esomeprazole, or pharmaceutically acceptable salt thereof, is released from said **AM and PM** unit dose **forms** [[**form**]] at a pH of ~~**from about**~~ 0 or greater, ~~**wherein one unit dose form is administered as an**~~

the AM **and PM unit** dose **forms** ~~**and a second dose administered about 10 hours later as a PM dose to**~~ target:

i) a pharmaceutical (pk) profile for naproxen where:

~~**a) the AM dose has a mean C_{max} of about 81 µg/mL and a median time to maximum concentration (T_{max}) of from about 2.5 to about 4 hours, and**~~

~~**b) the PM dose has a mean C_{max} of about 76.2 µg/mL and a median T_{max} of from about 10 to about 14 hours**~~

a) for the AM dose of naproxen, the mean C_{max} is 86.2 µg/mL (±20%) and the median T_{max} is 3.0 hours (±20%); and

b) for the PM dose of naproxen, the mean C_{max} is 76.8 µg/mL (±20%) and the median T_{max} is 10 hours (±20%); and

ii) a pharmacokinetic (pk) profile for esomeprazole where:

~~a) the AM dose has a mean area under the plasma concentration-time curve from time zero when the AM dose is administered to about 10 hours after the AM dose is administered ($AUC_{0\text{-}10,am}$) of about 850 hr*µg/mL, and~~

~~b) the PM dose has a mean area under the plasma concentration-time curve from time zero when the PM dose is administered to about 14 hours after the PM dose is administered ($AUC_{0\text{-}14,pm}$) of about 650 hr*µg/mL~~

a) for the AM dose of esomeprazole, the mean area under the plasma concentration-time curve from when the AM dose is administered to 10 hours (±20%) after the AM dose is administered ($AUC_{0\text{-}10,am}$) is 1216 hr*µg/mL (±20%),

b) for the PM dose of esomeprazole, the mean area under the plasma concentration-time curve from when the PM dose is administered to 14 hours (±20%) after the PM dose is administered ($AUC_{0\text{-}14,pm}$) is 919 hr*µg/mL (±20%), and

c) the total mean area under the plasma concentration-time curve for esomeprazole from when the AM dose is administered to 24 hours (±20%) after the AM dose is administered ($AUC_{0\text{-}24}$) is 2000 hr*µg/mL (±20%); and.

the AM and PM unit dose forms further target a mean % time at which intragastric pH remains at about 4.0 or greater for about a 24 hour period after reaching steady state that is at least about 60%.

Claims 20-28 (cancelled).

29. (**currently amended**) The method according to claim **[[27]] 19**, wherein the mean % time at which intragastric pH remains at about 4.0 or greater for about a 24 hour period after reaching steady state is at least about 71%.

Claims 30-32 (cancelled).

33. (**currently amended**) The method according to claim 19, wherein said **AM and PM** unit dose **forms are** ~~**form is**~~ administered for a period of at least about 6 days.

34. (**currently amended**) The method according to claim 19, wherein said **AM and PM** unit dose **forms are** ~~**form is**~~ administered for a period of at least about 9 days.

Claims 35-39 (cancelled).

40. (**currently amended**) The method according to claim 19, wherein said **AM and PM** unit dose **forms are each** ~~**form is**~~ a multilayer tablet comprising at least one core and at least a first layer and a second layer, wherein:

i) said core comprises naproxen, or pharmaceutically acceptable salt thereof;

ii) said first layer is a coating that at least begins to release the naproxen, or pharmaceutically acceptable salt thereof, when the pH of the surrounding medium is about 3.5 or greater; and

iii) said second layer comprises esomeprazole **or a pharmaceutically acceptable salt thereof**, wherein said esomeprazole **or salt thereof** is released at a pH of from ~~**about**~~ 0 or greater.

Claim 41 (cancelled).

42. (**currently amended**) The method according to claim 40, wherein said esomeprazole **or salt thereof** is released at a pH of from ~~**about**~~ 0 to about 2.

Claims 43 and 44 (cancelled).

45. (**previously presented**) The method according to claim 40, wherein said multi-layer tablet is substantially free of sodium bicarbonate.

Claims 46 and 47 (cancelled).

Remarks/Arguments

Applicants request reconsideration of this application on the merits.

I. Claim amendments

This amendment cancels claims 20-28, 30, 31, 38, and 39. Thus, claims 19, 29, 33, 34, 40, 42, and 45 are pending.

Claims 19, 29, 33, 34, 40, and 42 have been amended. Applicants submit the amendments do not introduce new matter. Specifically:

1. Claim 19 has been amended to incorporate the recitations in claims 20, 22, 25, and 28.
2. In several instances in claim 19, the term "about" has been replaced with "(±20%)". This amendment is supported Applicants' specification at, for example, page 6, lines 17-18. Claims 19, 40, and 42 have been amended to remove the "about" characterization of a pH of 0.
3. Claim 19 has been amended to recite the dosage amounts of naproxen (or a salt thereof) and esomeprazole (or a salt thereof). This amendment is supported by, for example, originally-filed claim 31; page 25, line 23 to page 26, line 4; and the pk results for PN400/E20 in Example 1, pages 46-53.
4. Claim 29 has been amended to depend from claim 19 rather than cancelled claim 27.
5. Claims 33 and 34 have been amended to more closely track the amended language in claim 19.
6. Claims 40 and 42 have been amended to expressly recite a salt of esomeprazole. This amendment makes the claims more consistent with amended claim 1.
7. Other amendments rephrase the claims or correct obvious errors.

Applicants reserve their right to pursue any subject matter cancelled or otherwise disclosed in this application in or more later-filed continuations and/or divisionals.

II. Response to rejection under 35 U.S.C. § 112 (First Paragraph)

Claims 19-31, 33, 34, 38-40, 42, and 45 have been rejected as lacking enablement. Specifically, the Office action asserts that the specification does not enable the delivery of

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