

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

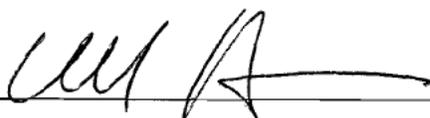
APPLICATION NUMBER:
202344Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

Statement Regarding Patent Litigation

EffRx Pharmaceuticals SA certifies that it has not been sued for patent infringement during the 45-day period provided for in section 505(c)(3)(C) of the act following the notification of the patent holders of Patent Nos. 5358941, 5681590, 6090410, and 6194004. Pursuant to 21 CFR Part 314.52(e), proof of patent notification was submitted to FDA in NDA 202344 Sequence 0003 on May 12, 2011.

Signature



Marshall A. Hayward, Ph.D.
Chief Scientific Officer
EffRx Pharmaceuticals SA
Biopole
Route de la Corniche 9B
CH-1066 Epalinges, Switzerland

Date

13 October 2011

EXCLUSIVITY SUMMARY

NDA # 202344

SUPPL #

HFD #

Trade Name Binosto

Generic Name alendronate sodium effervescent tablets

Applicant Name EffRx Pharmaceuticals SA

Approval Date, If Known March 12, 2012

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.

There are no clinical efficacy data presented in the application, as it is based upon demonstration of bioequivalence of Binosto 70 mg effervescent tablet to Fosamax 70 mg tablet.

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

d) Did the applicant request exclusivity?

YES NO

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

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

YES NO

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

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#s: 020560 021575 021762 | Fosamax Tablets Fosamax Oral Solution Fosamax Plus D |
| NDA# | ANDAs:019065, 079210, 090520, 090328, 076584, 076768 079049, 079109, 090932, 077982, 090258, 075710, 075711, 076184, 076984, 075871 076253 | alendronate sodium |
| NDA# | ANDAs:090139, 090741 | alendronate sodium and chloecalciferol |

2. Combination product.

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

YES NO

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

NDA#

NDA#

NDA#

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

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

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

YES NO

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

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

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

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 # YES ! NO
! Explain:

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

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

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

/s/

MEREDITH ALPERT
03/12/2012

AUDREY L GASSMAN
03/12/2012

PEDIATRIC PAGE
(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 202344 Supplement Number: _____ NDA Supplement Type (e.g. SE5): _____
Division Name: DRUP PDUFA Goal Date: _____ Stamp Date: 12/22/2010
December 15, 2011

Proprietary Name: TBD
Established/Generic Name: alendronate sodium effervescent tablets, 70 mg
Dosage Form: tablet
Applicant/Sponsor: EffRx Pharmaceuticals SA

Indication(s) previously approved (please complete this question for supplements and Type 6 NDAs only):

- (1) _____
(2) _____
(3) _____
(4) _____

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 2
(Attach a completed Pediatric Page for each indication in current application.)

Indication: treatment of postmenopausal osteoporosis

Q1: Is this application in response to a PREA PMR? Yes Continue
No Please proceed to Question 2.

If Yes, NDA/BLA#: _____ Supplement #: _____ PMR #: _____

Does the division agree that this is a complete response to the PMR?

- Yes. Please proceed to Section D.
 No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

Q2: Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW active ingredient(s) (includes new combination); indication(s); dosage form; dosing regimen; or route of administration?*

(b) No. PREA does not apply. **Skip to signature block.**

*** Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.**

Q3: Does this indication have orphan designation?

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

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

- Yes: (Complete Section A.)
 No: Please check all that apply:
 Partial Waiver for selected pediatric subpopulations (Complete Sections B)
 Deferred for some or all pediatric subpopulations (Complete Sections C)
 Completed for some or all pediatric subpopulations (Complete Sections D)
 Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
 Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (check, and attach a brief justification for the reason(s) selected)

- Necessary studies would be impossible or highly impracticable because:
 - Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____
- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)

Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

| | | Reason (see below for further detail): | | | | | |
|--------------------------|---------|--|---------------|---------------------------|-------------------------------------|------------------------------------|---------------------------------|
| | | minimum | maximum | Not feasible [#] | Not meaningful therapeutic benefit* | Ineffective or unsafe [†] | Formulation failed ^Δ |
| <input type="checkbox"/> | Neonate | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Reason(s) for partial waiver (check reason corresponding to the category checked above, and attach a brief justification):

Not feasible:

- Necessary studies would be impossible or highly impracticable because:
 - Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____

Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpmhs@fda.hhs.gov) OR AT 301-796-0700.

pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.*)

Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for selected pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

| Deferrals (for each or all age groups): | | | | Reason for Deferral | | | Applicant Certification † |
|--|---------------|---------------|--------------------------|------------------------------|---|---|---------------------------|
| | | | | Ready for Approval in Adults | Need Additional Adult Safety or Efficacy Data | Other Appropriate Reason (specify below)* | Received |
| Population | minimum | maximum | | | | | |
| <input type="checkbox"/> Neonate | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| <input type="checkbox"/> Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| <input type="checkbox"/> Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| <input type="checkbox"/> Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| <input type="checkbox"/> Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| <input type="checkbox"/> All Pediatric Populations | 0 yr. 0 mo. | 16 yr. 11 mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| Date studies are due (mm/dd/yy): _____ | | | | | | | |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpms@fda.hhs.gov) OR AT 301-796-0700.

* Other Reason: _____

+ Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

| Pediatric subpopulation(s) in which studies have been completed (check below): | | | | | |
|--|------------------------------|---------------|---------------|---|-----------------------------|
| Population | | minimum | maximum | PeRC Pediatric Assessment form attached?. | |
| <input type="checkbox"/> | Neonate | __ wk. __ mo. | __ wk. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | All Pediatric Subpopulations | 0 yr. 0 mo. | 16 yr. 11 mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

| Population | | minimum | maximum |
|--------------------------|------------------------------|---------------|---------------|
| <input type="checkbox"/> | Neonate | __ wk. __ mo. | __ wk. __ mo. |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> | All Pediatric Subpopulations | 0 yr. 0 mo. | 16 yr. 11 mo. |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

| Population | | minimum | maximum | Extrapolated from: | |
|--------------------------|------------------------------|---------------|---------------|--------------------------|--------------------------|
| | | | | Adult Studies? | Other Pediatric Studies? |
| <input type="checkbox"/> | Neonate | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | All Pediatric Subpopulations | 0 yr. 0 mo. | 16 yr. 11 mo. | <input type="checkbox"/> | <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpms@fda.hhs.gov) OR AT 301-796-0700.

If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

Karl Stiller

Regulatory Project Manager

(Revised: 6/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.

Attachment A

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

Indication #2: increase bone mass in men with osteoporosis**Q1:** Does this indication have orphan designation?

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

Q2: Is there a full waiver for all pediatric age groups for this indication (check one)?

- Yes: (Complete Section A.)
- No: Please check all that apply:
- Partial Waiver for selected pediatric subpopulations (Complete Sections B)
 - Deferred for some or all pediatric subpopulations (Complete Sections C)
 - Completed for some or all pediatric subpopulations (Complete Sections D)
 - Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
 - Extrapolation in One or More Pediatric Age Groups (Complete Section F)
- (Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

- Necessary studies would be impossible or highly impracticable because:
- Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____
- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

 Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

| | | | Reason (see below for further detail): | | | | |
|--------------------------|---------|---------------|--|---|------------------------------------|---------------------------------|--------------------------|
| | minimum | maximum | Not feasible [#] | Not meaningful therapeutic benefit [*] | Ineffective or unsafe [†] | Formulation failed ^Δ | |
| <input type="checkbox"/> | Neonate | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief justification**):

Not feasible:

- Necessary studies would be impossible or highly impracticable because:
 - Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____

* Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Section C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so,

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpmhs@fda.hhs.gov) OR AT 301-796-0700.

proceed to Section F).. Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for some or all pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

| Deferrals (for each or all age groups): | | | | Reason for Deferral | | | Applicant Certification † |
|---|---------------------------|---------------|---------------|------------------------------|---|---|---------------------------|
| Population | | minimum | maximum | Ready for Approval in Adults | Need Additional Adult Safety or Efficacy Data | Other Appropriate Reason (specify below)* | Received |
| <input type="checkbox"/> | Neonate | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | All Pediatric Populations | 0 yr. 0 mo. | 16 yr. 11 mo. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Date studies are due (mm/dd/yy): _____ | | | | | | | |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

* Other Reason: _____

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

pediatric subpopulation(s) in which studies have been completed (check below):

| Population | | minimum | maximum | PeRC Pediatric Assessment form attached? | |
|--------------------------|------------------------------|---------------|---------------|--|-----------------------------|
| <input type="checkbox"/> | Neonate | __ wk. __ mo. | __ wk. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| <input type="checkbox"/> | All Pediatric Subpopulations | 0 yr. 0 mo. | 16 yr. 11 mo. | Yes <input type="checkbox"/> | No <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

| Population | | minimum | maximum |
|--------------------------|------------------------------|---------------|---------------|
| <input type="checkbox"/> | Neonate | __ wk. __ mo. | __ wk. __ mo. |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> | Other | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> | All Pediatric Subpopulations | 0 yr. 0 mo. | 16 yr. 11 mo. |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

*Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition **AND** (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.*

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

| Population | minimum | maximum | Extrapolated from: | |
|---|---------------|---------------|--------------------------|--------------------------|
| | | | Adult Studies? | Other Pediatric Studies? |
| <input type="checkbox"/> Neonate | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> Other | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> All Pediatric Subpopulations | 0 yr. 0 mo. | 16 yr. 11 mo. | <input type="checkbox"/> | <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

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

Reason(s) for waiving pediatric assessment requirements:

For both indications:

- a. Studies are impossible or highly impractical (e.g. the number of pediatric patients is so small or is geographically dispersed). If applicable, chose from adult-related conditions in Attachment I

Justification for indication 1: Postmenopausal Osteoporosis; studies are impossible given the lack of pediatric patients with these conditions

Justification for indication 2: Studies are impossible given the lack of pediatric patients with these conditions

This page was completed by:

See appended electronic signature page}

Karl Stiller

Regulatory Project Manager

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

(Revised: 6/2008)



EffRx Pharmaceuticals S.A.

DEBARMENT CERTIFICATION

EffRx Pharmaceuticals SA hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug, and Cosmetic Act in connection with the new drug application, NDA 202344, for Alendronate Sodium 70 mg Effervescent Tablets.

Signature

A handwritten signature in black ink, appearing to read 'M. Hayward', written over a horizontal line.

Marshall A. Hayward, Ph.D.
Chief Scientific Officer
EffRx Pharmaceuticals SA
Biopole
Route de la Corniche 4
CH-1066 Epalinges S / Lausanne
Switzerland

Date

8 December 2010

ACTION PACKAGE CHECKLIST

| APPLICATION INFORMATION ¹ | | |
|---|--------------------------------------|--|
| NDA # 202344 BLA # | NDA Supplement # BLA Supplement # | If NDA, Efficacy Supplement Type: Original |
| Proprietary Name: Binosto Established/Proper Name: alendronate sodium Dosage Form: Effervescent Tablets | | Applicant: EffRx Pharmaceuticals SA Agent for Applicant (if applicable): Hurley Consulting |
| RPM: Meredith Alpert | | Division: Division of Reproductive and Urologic Products |
| <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><u>NDA and NDA Efficacy Supplements:</u></p> <p>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> </div> <div style="width: 50%;"> <p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Fosamax (alendronate sodium) Tablets, 70 mg (NDA 20560)</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>dosage form</p> <p><input type="checkbox"/> This application does not rely upon a listed drug. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input checked="" type="checkbox"/> This application relies on (explain) the findings of safety and efficacy of Fosamax Tablets, 70 mg.</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: March 12, 2012</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> </div> </div> | | |
| ❖ Actions | | |
| <ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>March 15, 2012</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 |

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.

² For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

| | |
|---|--|
| <p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: 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 _____</p> | <p><input type="checkbox"/> Received</p> |
| <p>❖ Application Characteristics ³</p> | |
| <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>NDA: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies</p> <p>BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <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>REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input checked="" type="checkbox"/> MedGuide w/o REMS <input checked="" type="checkbox"/> REMS not required</p> <p>Comments:</p> | |
| <p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p> | <p><input type="checkbox"/> Yes, dates</p> |
| <p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p> | <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> |
| <p>❖ Public communications (<i>approvals only</i>)</p> | |
| <ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action | <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</p> |
| <ul style="list-style-type: none"> Press Office notified of action (by OEP) | <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</p> |
| <ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated | <p><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</p> |

³ 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.

| ❖ 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 type="checkbox"/> N/A (no paragraph IV certification) <input checked="" 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).

| | |
|---|---|
| <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 checked="" type="checkbox"/> No |
|---|---|

CONTENTS OF ACTION PACKAGE

| | | |
|---|--|--|
| ❖ Copy of this Action Package Checklist ⁴ | | |
| 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) Approval, 3/12/2012 |
| 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. | | 3/8/2012 |
| <ul style="list-style-type: none"> • Original applicant-proposed labeling | | 12/22/2010 |
| <ul style="list-style-type: none"> • Example of class labeling, if applicable | | N/A |

⁴ Fill in blanks with dates of reviews, letters, etc.

| | |
|--|--|
| <ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<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"/> Device Labeling <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. | 3/5/2012 |
| <ul style="list-style-type: none"> • Original applicant-proposed labeling | 12/22/2010 |
| <ul style="list-style-type: none"> • Example of class labeling, if applicable | N/A |
| <ul style="list-style-type: none"> ❖ 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 | 3/5/2012 |
| <ul style="list-style-type: none"> ❖ 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>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. | letters: 5/11/11 and 9/9/11 reviews: 5/3/11, 9/9/11, 11/8/11, 2/9/11 |
| <ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) | <input checked="" type="checkbox"/> RPM 4/15/11 <input checked="" type="checkbox"/> DMEPA 2/7/12 <input checked="" type="checkbox"/> DMPP/PLT (DRISK) 2/28/12 <input checked="" type="checkbox"/> ODPD (DDMAC) 2/29/12, 2/23/12 <input checked="" type="checkbox"/> SEALD 3/8/12 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews |
| Administrative / Regulatory Documents | |
| <ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) | <input type="checkbox"/> Not a (b)(2) 2/27/12 <input type="checkbox"/> Not a (b)(2) 3/12/12 |
| <ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) | <input checked="" type="checkbox"/> Included |
| <ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm | |
| <ul style="list-style-type: none"> • Applicant is 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 |
| <ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>10/5/12</u> If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) | <input checked="" type="checkbox"/> Included |

⁵ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

| | |
|--|---|
| ❖ 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, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)</i> | 12/27/10, 2/18/11, 4/28/11, 5/11/11, 7/21/11, 7/27/11, 8/30/11, 9/9/11, 9/21/11, 10/12/11, 10/31/11, 11/14/11, 2/16/12 (3), 2/17/12 |
| ❖ Internal memoranda, telecons, etc. | None |
| ❖ 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 9/1/10 |
| • EOP2 meeting <i>(indicate date of mtg)</i> | <input checked="" type="checkbox"/> No mtg |
| • Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i> | |
| ❖ 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 3/12/12 |
| Cross-Discipline Team Leader Review <i>(indicate date for each review)</i> | <input type="checkbox"/> None 2/24/12 |
| PMR/PMC Development Templates <i>(indicate total number)</i> | <input checked="" type="checkbox"/> None |
| Clinical Information⁶ | |
| ❖ Clinical Reviews | |
| • Clinical Team Leader Review(s) <i>(indicate date for each review)</i> | 2/24/12 |
| • Clinical review(s) <i>(indicate date for each review)</i> | 2/7/12 |
| • 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> | 4/28/11 |
| ❖ Clinical reviews from immunology and other clinical areas/divisions/Centers <i>(indicate date of each review)</i> | <input checked="" type="checkbox"/> None |
| ❖ Controlled Substance Staff review(s) and Scheduling Recommendation <i>(indicate date of each review)</i> | <input checked="" type="checkbox"/> Not applicable |

⁶ Filing reviews should be filed with the discipline reviews.

| | |
|---|--|
| ❖ Risk Management <ul style="list-style-type: none"> REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>) REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) 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 checked="" type="checkbox"/> None requested |
| 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 | |
| ❖ 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 9/12/11 |
| 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 2/9/12, 3/8/12 |
| ❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>) | <input type="checkbox"/> None 10/7/11, 9/27/11, 5/6/11 |
| 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 checked="" type="checkbox"/> None |
| • Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>) | <input type="checkbox"/> None 2/9/12 |
| ❖ 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 Included in P/T review, page |
| ❖ 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 type="checkbox"/> None 10/13/11, 3/7/12 |
| • Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i> | | <input type="checkbox"/> None 9/19/11, 10/23/11 |
| ❖ Microbiology Reviews | | <input checked="" type="checkbox"/> Not needed |
| <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 (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i> | | |
| ❖ 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)(all original applications and all efficacy supplements that could increase the patient population)</i> | | |
| <input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i> | | |
| <input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i> | | |
| ❖ Facilities Review/Inspection | | |
| <input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷)</i> | | Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input checked="" type="checkbox"/> Not applicable |
| <input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</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 type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review) |

⁷ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

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.

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/s/

MEREDITH ALPERT
03/15/2012

From: Alpert, Meredith
To: ["Mondabaugh, Susan"](#)
Subject: NDA 202344 Binosto CMC commitment
Date: Monday, February 27, 2012 12:12:00 PM

Hi Sue,

We acknowledge your commitment to update your drug product with an imprint within one year of the action date. However, after further internal discussion, because of safety concerns with having an unmarked tablet on the market, we request that you make the following commitments:

1. Unmarked product will not be introduced into interstate commerce as per 21 CFR 206.10
2. Prior to marketing, submit a CBE-30 supplement to provide updated information on the marked tablets including
 - diagrams for the die
 - an updated manufacturing process
 - revised labeling updating the HOW SUPPLIED and DOSAGE FORMS AND STRENGTHS sections and SPL
 - an updated specification sheet with revised APPEARANCE acceptance criteria
 - full release testing for the new batch, including disintegration testing
3. Place the first marked batch on stability and update the stability data in the next Annual Report

Thank you,

Meredith Alpert, M.S.
Acting Safety Regulatory Project Manager
Center for Drug Evaluation and Research
Office of New Drugs
Division of Reproductive and Urologic Products
Phone: 301-796-1218, Fax: 301-796-9897
Email: meredith.alpert@fda.hhs.gov

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/s/

MEREDITH ALPERT
02/27/2012



NDA 202344

**ACKNOWLEDGE CORPORATE
ADDRESS CHANGE**

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

We acknowledge receipt on February 16, 2012, of your February 16, 2012, correspondence notifying the Food and Drug Administration (FDA) that the corporate address has been changed from

EffRx Pharmaceuticals SA
Biopole
Route de la Corniche 9B
CH- 1066 Epalinges
Switzerland

to

EffRx Pharmaceuticals SA
Wolleraustrasse 41B
CH-8807 Freienbach
Switzerland

for the following new drug application (NDA):

NDA 202344 for alendronate sodium effervescent tablets, 70 mg.

We have revised our records to reflect this change.

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

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

If you have any questions, call me, at (301) 796-1218.

Sincerely,

{See appended electronic signature page}

Meredith Alpert, M.S.
Regulatory Health Project Manager
Division of Reproductive and Urologic
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MEREDITH ALPERT
02/17/2012

From: Alpert, Meredith
To: "[Mondabaugh, Susan](#)"
Subject: NDA 202344 (Binosto) PI
Date: Thursday, February 16, 2012 12:51:00 PM
Attachments: [binostopi_FDAedits021612_marked.doc](#)
[binostopi_FDAedits021612_clean.doc](#)
[Binosto_labeling_fda_edits.doc](#)

Dear Sue,

Attached are three documents regarding your Physician Insert. The documents are the following:

- 1) PI containing track changes
- 2) PI (clean version with no track changes)
- 3) PI justification document

If you have any questions, please contact me. We are requesting a one week response turnaround time. Please confirm receipt by replying to this email.

Regards,

Meredith Alpert, M.S.
Acting Safety Regulatory Project Manager
Center for Drug Evaluation and Research
Office of New Drugs
Division of Reproductive and Urologic Products
Phone: 301-796-1218, Fax: 301-796-9897
Email: meredith.alpert@fda.hhs.gov

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/s/

MEREDITH ALPERT
02/16/2012

From: Alpert, Meredith
To: ["Mondabaugh, Susan"](#)
Subject: Amendment to labeling comments letter (NDA 202344)
Date: Thursday, February 16, 2012 9:18:00 AM

Hi Sue,

An error was discovered in the first comment under General Comments of the letter for NDA 202344 (Binosto). Please amend that particular comment with the following:

The established name for Binosto is "alendronate sodium" and not "Alendronate Sodium" with A and S in capital letters as shown in the 1st comment to the applicant.

Thank you,
Meredith Alpert, M.S.
Acting Safety Regulatory Project Manager
Center for Drug Evaluation and Research
Office of New Drugs
Division of Reproductive and Urologic Products
Phone: 301-796-1218, Fax: 301-796-9897
Email: meredith.alpert@fda.hhs.gov

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/s/

MEREDITH ALPERT
02/16/2012



NDA 202344

LABELING PMR/PMC DISCUSSION COMMENTS

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for alendronate sodium effervescent tablets, 70 mg.

We also refer to our November 14, 2011, letter in which we notified you regarding the communication of labeling changes and/or postmarketing requirements/commitments in accordance with the "PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES – FISCAL YEARS 2008 THROUGH 2012."

We have the following comments regarding your packaging:

General Comments:

1. Present the proprietary name in title case as "Binosto" and the established name as "(Alendronate Sodium) Effervescent Tablets".
2. Include a United States point of contact for questions and adverse event reporting.

Container Label (Blister):

1. Clarify if each blister contains 1 effervescent tablet or multiple effervescent tablets. As currently presented, each blister is labeled as "Effervescent Tablets."
2. Ensure that "Lot #" instead of the batch number is printed on the back side of the blister along with the expiration date per 21 CFR 201.10(i).

Pouch Labeling:

1. Replace the (scissors symbol) with the word "cut" so that the instruction is stated clearly and reduces the risk of misinterpreting the proposed symbol.
2. Clarify if each pouch contains 1 effervescent tablet or multiple effervescent tablets. As currently presented, each pouch is labeled as "Effervescent Tablets."

Carton Labeling:

1. Include the statement of dosage such as “Usual dose: see prescribing information” per 21 CFR 201.55.
2. Relocate the NDC number to the top third of the principal display panel of the label per 21 CFR 207.35(b)(3).
3. Clarify whether the Medication Guide is accompanied on the carton or enclosed inside the carton. As currently presented, the statement “Pharmacist: Dispense the accompanying Medication Guide...” on the principal display panel and the statement “Important Information: Please read the enclosed Medication Guide...” on the back panel convey different messages.
4. Revise the Medication Guide statement on the principal display panel to read “ATTENTION PHARMACIST: Each patient is required to receive the accompanying/enclosed Medication Guide” and increase its prominence per 21 CFR 208.24(d) (Clarify between accompany or enclosed, see Comment D3).

If you have any questions, call me at (301) 796-1218.

Sincerely,

{See appended electronic signature page}

Meredith Alpert, M.S.
Regulatory Health Project Manager
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MEREDITH ALPERT
02/16/2012



NDA 202344

**REVIEW EXTENSION –
MAJOR AMENDMENT**

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for alendronate sodium effervescent tablets, 70 mg.

On October 28, 2011, we received your October 27, 2011, solicited major amendment to this application. The receipt date is within three months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is March 15, 2012.

In addition, we are establishing a new timeline for communicating labeling changes and/or postmarketing requirements/commitments in accordance with "PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES – FISCAL YEARS 2008 THROUGH 2012." If major deficiencies are not identified during our review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by February 4, 2012.

If you have any questions, call Meredith Alpert, Regulatory Project Manager, at (301) 796-1218.

Sincerely,

{See appended electronic signature page}

Margaret M. Kober, R.Ph.,M.P.A.
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MARGARET M KOBER
11/14/2011
Chief, Project Management Staff

From: Alpert, Meredith
To: ["Mondabaugh, Susan";](#)
Subject: NDA 202344 comments
Date: Monday, October 31, 2011 11:02:00 AM

Hi Sue,

I just listened to your voicemail from last week. Below are more comments for you regarding the carton and container from chemistry. I will convey to DMEPA that you do not have a label blister available and ask them what would be acceptable in its place. Please respond to this email to confirm receipt.

1) All labeling including blister, carton and sleeve.

- The established name and dosage form should be printed as follows:

(alendronate sodium) Effervescent Tablets

- The font size of established name, dosage form and dosage administration should be at least 50% of the proprietary name.

- Update NDC numbers.

2) Blister label

- Print the name of the manufacturer/distributor.

- Print the NDC number

- Print the barcode

4) Carton label

- Storage condition should be correctly described as:

“Store at 25°C (77°F), excursions permitted to 15°C - 30°C (59°F - 86°F) [See USP Controlled Room Temperature]”

5) Sleeve

- Indicate the total number of tablets e. g. Total 12 Effervescent Tablets.

- Print lot number and expiration date.

Meredith Alpert, M.S.

Acting Safety Regulatory Project Manager

Center for Drug Evaluation and Research

Office of New Drugs

Division of Reproductive and Urologic Products

Phone: 301-796-1218, Fax: 301-796-9897

Email: meredith.alpert@fda.hhs.gov

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/s/

MEREDITH H ALPERT
10/31/2011

MEMORANDUM OF MEETING MINUTES

Meeting Type: Teleconference to convey comments
Meeting Category: NDA
Meeting Date and Time: October 12, 2011, 11:00 –11:30 a.m. EST
Meeting Location: Teleconference
Application Number: NDA 202344
Product Names: Binosto (conditionally accepted)
Indications: Osteoporosis
Sponsor/Applicant Name: EffRX (Hurley Consulting Agency)
Meeting Chair: Theresa Kehoe, M.D.
Meeting Recorder: Meredith Alpert, M.S.

FDA ATTENDEES

Theresa Kehoe, M.D. – Clinical Team Leader, DRUP
Stephen Voss, M.D. – Medical Officer, DRUP
Hyunjin Kim, Pharm.D. – Clinical Pharmacology Reviewer, Division of Clinical Pharmacology III (DCPIII), Office of Clinical Pharmacology (OCP) at DRUP
Meredith Alpert, M.S.–Regulatory Project Manager, DRUP

SPONSOR ATTENDEES

Sue Mondabaugh, PhD, VP Regulatory Affairs, Hurley Consulting Associates Ltd.
Margaret E. Hurley, MD, President & CEO, Hurley Consulting Associates Ltd.
Marshall Hayward, PhD, Chief Scientific Officer, EffRx Pharmaceuticals SA

BACKGROUND

The pre-approved NDA was submitted on February 15, 2011. On September 27, 2011, the Bioequivalence Establishment Inspection Report Review was completed. The analytical portion of the study was conducted at (b) (4). Following inspection of (b) (4) a form FDA 483, citing the observations during the inspection was issued. The observations listed a deficiency and recommendations on how to correct the deficiencies listed in the 483 form. On October 12, 2011, the division initiated a teleconference with the applicant in order to convey the deficiencies and recommendations to the applicant listed in the 483 form.

DISCUSSION

The applicant acknowledged that they were aware of the 483 issued to (b) (4). The division began the meeting by conveying stating that these findings raised concerns regarding the adequacy of the bioequivalence findings for the NDA. While 13 batches

are outlined in the 483, only two batches were reassayed and the other 11 were reported without reassay. Therefore, the 11 batches that were not re-assayed are the issue. The Division proposed a two step plan for reanalysis of the bioequivalence data. First, perform a statistical reanalysis of the bioequivalence data with the 11 batches outlined in the 483 removed. If bioequivalence is maintained, then no further samples reassay is necessary. However, if BE criteria are not maintained after the removal of the 11 batches, then reassay of those 11 batches of urine samples would be necessary.

The applicant asked if they needed to reanalyze the urine samples. The division responded by clarifying that the applicant just needed to redo the statistical analysis excluding the 11 runs and if they still met the BE criteria, the division would be satisfied. However, if they do not meet the BE criteria after the removal of the 11 runs, the option to reanalyze the other 11 urine samples is still available. The applicant asked for confirmation that if they perform a statistical analysis and the BE criteria is met that the division would be satisfied. The division confirmed that this would be the case.

The division asked the applicant for a 2-week turnaround time maximum. The applicant responded that it was a reasonable request. The division further asked that the applicant submit all of the raw data sets in the SAS transport file, tables and figures. The applicant agreed to do so. The applicant asked how long it would take for the division to review the data, and the division responded that it depends on the amount of data that needs to be reviewed internally. The applicant concluded the meeting by stating they would do their best to meet our requested timelines.

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/s/

MEREDITH H ALPERT
11/09/2011

From: Alpert, Meredith
To: ["Mondabaugh, Susan";](#)
Subject: NDA 202344 carton comments
Date: Wednesday, October 12, 2011 12:17:00 PM
Attachments: [Binosto image for reference.pdf](#)

Hi Sue,

I have been asked to share the following comments from DMEPA regarding your carton. Please also see attached image for reference:

In our initial phase of our labeling review, DMEPA identified a design issue. Our preliminary evaluation finds the design of the proposed carton introduces vulnerability that can lead to medication errors (See attached carton labeling image for reference).

1. The instructions on the rear, Panel 4 are confusing because when reading left to right and then top to bottom, the text reads (Week 2, Week 1, Week 3, Week 4).
2. Panel 4 has multiple "Step 1" and "Step 3" instructions associated with each week. However, "Opening Steps: 1 to 5" are not associated with a specific week. Additionally, the overlapping "Step 1" and "Opening Steps: 1 through 5" instructions are confusing as to which "Step" is truly the first step.
3. Instructions for removing the pouch are displayed on two opposing panels, thus causing confusion as users would have to flip the carton back and forth, starting on the rear Panel 4, in order to read and follow the instructions.
4. The text on Panel 4 appears in both a vertical and horizontal orientation which decreases readability.

Recommendations:

If you have usability data to support that representative users can adequately use this carton design, please submit for review.

If no data is available, redesign the carton with simpler instructions for use. Consider presenting the weekly doses vertically such that upon flipping the carton from Panel 3 to Panel 4 does not alter the week order.

Additionally, we have concerns regarding the text on the container label and carton labeling; however, these concerns will be addressed in a separate review.

Meredith Alpert, M.S.
Acting Safety Regulatory Project Manager
Center for Drug Evaluation and Research
Office of New Drugs
Division of Reproductive and Urologic Products
Phone: 301-796-1218, Fax: 301-796-9897
Email: meredith.alpert@fda.hhs.gov

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/s/

MEREDITH H ALPERT
10/12/2011

Alpert, Meredith

From: Greeley, George
Sent: Thursday, October 06, 2011 8:23 AM
To: Alpert, Meredith
Cc: Mathis, Lisa; Addy, Rosemary; Suggs, Courtney; Lee, Catherine S.; Monroe, Scott
Subject: NDA 202-344 Binosto

Importance: High

Attachments: 1_Pediatric_Record.pdf

Hi Meredith,

This email serves as confirmation of the review for Binosto (Alendronate Sodium) conducted by the PeRC PREA Subcommittee on October 5, 2011.

The Division presented a full waiver in pediatric patients for the indications of treatment of postmenopausal osteoporosis and treatment to increase bone mass in men with osteoporosis because the disease/condition does not exist in children.

The PeRC agreed with the Division to grant a full waiver for this product.

The pediatric record is attached for Binosto.



*_Pediatric_Record
.pdf (66 KB)...

Thanks,

George Greeley
Regulatory Health Project Manager
Pediatric and Maternal Health Staff
FDA/CDER/OND
10903 New Hampshire Avenue
Bldg. 22, Room 6467
Silver Spring, MD 20993-0002
Phone: 301.796.4025
Email: george.greeley@fda.hhs.gov

Please consider the environment before printing this e-mail.



NDA 202-344

GENERAL ADVICE

EffRx Pharmaceuticals SA
Agent: Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D., FRAPS, VP Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Steovess™ (alendronate sodium) Effervescent Tablet.

We have reviewed the referenced material and have the following recommendation:

Your proposed disintegration method (in water, 20°C) is acceptable; however, we recommend that the proposed disintegration acceptance criteria be revised as follows:

Change from:

[Redacted] (b) (4)

To: [Redacted] (b) (4)

If you have any questions, call Becky McKnight, Regulatory Project Manager, at (301) 796-1765.

Sincerely,

{See appended electronic signature page}

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

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/s/

MOO JHONG RHEE
09/21/2011
Chief, Branch IV



NDA 202344

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

EffRx Pharmaceuticals SA
c/o Hurley Consulting Associates Ltd.
One Main Street
Chatham, NJ 07928

ATTENTION: Susan M. Mondabaugh, PhD, FRAPS
Vice President, Regulatory Affairs

Dear Dr. Mondabaugh:

Please refer to your New Drug Application (NDA) dated December 21, 2010, received December 22, 2010, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Alendronate Sodium Effervescent Tablets, 70 mg.

We also refer to your June 21, 2011, correspondence, received June 22, 2011, requesting review of your proposed proprietary name, Binosto. We have completed our review of the proposed proprietary name, Binosto and have concluded that it is acceptable.

The proposed proprietary name, Binosto, 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 22, 2011 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 Maria Wasilik, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Meredith Alpert at (301) 796-1218.

Sincerely,

{See appended electronic signature page}

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

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/s/

CAROL A HOLQUIST
09/09/2011



NDA 202344

INFORMATION REQUEST

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for alendronate sodium effervescent tablets, 70 mg.

FDA investigators have identified significant violations to the bioavailability and bioequivalence requirements of Title 21, Code of Federal Regulation, Part 320 in bioanalytical studies conducted by Cetero Research in Houston, Texas (Cetero).¹ The pervasiveness and egregious nature of the violative practices by Cetero has led FDA to have significant concerns that the bioanalytical data generated at Cetero from April 1, 2005 to June 15, 2010, as part of studies submitted to FDA in New Drug Applications (NDA) and Supplemental New Drug Applications (sNDA) are unreliable. FDA has reached this conclusion for three reasons: (1) the widespread falsification of dates and times in laboratory records for subject sample extractions, (2) the apparent manipulation of equilibration or “prep” run samples to meet pre-determined acceptance criteria, and (3) lack of documentation regarding equilibration or “prep” runs that prevented Cetero and the Agency from determining the extent and impact of these violations.

Serious questions remain about the validity of any data generated in studies by Cetero Research in Houston, Texas during this time period. In view of these findings, FDA is informing holders of approved and pending NDAs of these issues.

The impact of the data from these studies (which may include bioequivalence, bioavailability, drug-drug interaction, specific population, and others) cannot be assessed without knowing the details regarding the study and how the data in question were considered in the overall development and approval of your drug product. At this time, the Office of New Drugs is searching available documentation to determine which NDAs are impacted by the above findings.

¹ These violations include studies conducted by Bioassay Laboratories and BA Research International specific to the Houston, Texas facility.

To further expedite this process, we ask that you inform us if you have submitted any studies conducted by Cetero Research in Houston, Texas during the time period of concern (April 1, 2005 to June 15, 2010). Please submit information on each of the studies, including supplement number (if appropriate), study name/protocol number, and date of submission. With respect to those studies, you will need to do one of the following: (a) re-assay samples if available and supported by stability data, (b) repeat the studies, or (c) provide a rationale if you feel that no further action is warranted.

Please respond to this query within 30 days from the date of this letter.

This information should be submitted as correspondence to your NDA. In addition, please provide a desk copy to:

Office of New Drugs
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Room 6300
Silver Spring, MD 20993-0002

If you have any questions, call Meredith Alpert, Regulatory Project Manager, at (301) 796-1218.

Sincerely,

{See appended electronic signature page}

Scott Monroe, M.D.
Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MARGARET M KOBER
08/30/2011
signed for Scott Monroe



NDA 202344

ACKNOWLEDGE ADDRESS CHANGE

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

We acknowledge receipt on June 27, 2011, of your June 27, 2011 correspondence notifying the Food and Drug Administration that the corporate name and/or address has been changed from

EffRx Pharmaceuticals SA
Biopole
Route de la Corniche 4
CH-1066 Epalinges S
Lausanne, Switzerland

to

EffRx Pharmaceuticals SA
Biopole
Route de la Corniche 9B
CH- 1066 Epalinges
Switzerland

for the following new drug application:

NDA 202344 for alendronate sodium effervescent tablets, 70 mg.

We have revised our records to reflect this change.

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

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

If you have any questions, call me, at (301) 796-1993.

Sincerely,

{See appended electronic signature page}

Karl Stiller, R.Ph.
Regulatory Health Project Manager
Division of Reproduction and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

KARL J STILLER
07/27/2011



NDA 202344

INFORMATION REQUEST

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

Please refer to your New Drug Application (NDA) dated December 21, 2010, received February 15, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for alendronate sodium effervescent tablets, 70mg.

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

- On the page 35 of the protocol AE-1212-001-EM, section 7.3.1 states that the effervescent solutions will be prepared no longer than 15 minutes and not less than 5 minutes before administration. Provide the detailed explanation of this “preparation” step (e.g., waiting without stirring, stirring).
- Provide the pharmacokinetic analysis of alendronate in males only with relevant tables (pharmacokinetic parameters and bioequivalence analysis) and figures (individual cumulative urinary excretion, geometric mean cumulative urinary excretion, geometric mean of the urinary excretion in linear Y-scale, and geometric mean of the urinary excretion in logarithmic Y-scale)
- Provide the means and standard deviations of data points in figures (geometric mean cumulative urinary excretion, geometric mean of the urinary excretion in linear Y-scale, and geometric mean of the urinary excretion in logarithmic Y-scale) for females only, males only, and females and males together in SAS transport file format.

If you have any questions, call George Lyght, Regulatory Project Manager, at (301) 796-0948.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph., M.P.A.
Chief, Project Management Staff
Division of Reproduction and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MARGARET M KOBER
07/21/2011
Chief, Project Management Staff

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEETING DATE: May 12, 2011
TIME: 11:00 – 11:30 am
LOCATION: WO 22 Room 5440
APPLICATION: IND 103130, NDA 202344
DRUG NAME: Avalent (Secondary proposed name)
TYPE OF MEETING: Proposed Proprietary Name

APPLICANT: EffRx Pharmaceuticals

MEETING CHAIR:

MEETING RECORDER:

FDA ATTENDEES:

Carlos M. Mena-Grillasca, Team Leader, DMEPA
Chi-Ming (Alice) Tu, Pharm.D., Safety Evaluator, DMEPA
Chris Wheeler, Team Leader, Project Management Staff, OSE
Maria Wasilik, Project Manager, OSE
Mark Liberatore, Project Manager, OSE
Ermias Zerislassie, Project Manager, OSE

EXTERNAL CONSTITUENT ATTENDEES:

Sue Mondabaugh, Regulatory Affairs
Margaret Hurley, MD, Regulatory Affairs
Marshall Hayward, PhD, Chief Scientific Officer, EffRx Pharmaceuticals SA

Background:

DMEPA requested this teleconference to inform the Sponsor of preliminary concerns identified during the review of the proposed proprietary name, Steovess, and the alternate name, Avalent.

Discussion

DMEPA's Findings:

We set up this courtesy call to notify you of our preliminary safety concerns with regards to your proposed secondary name, Avalent.

It is the FDA's policy to review only the primary name submission. However, we are calling you today regarding your secondary name in the intent of transparency.

Our preliminary review of the proposed name Avalent has identified that the name may not be acceptable for the following reason:



Since you recently received an unacceptable letter for your proposed primary name, Steovess, we wanted to present you with your regulatory option.

Only choice: Submit an alternative name for review.

Please keep in mind that every proprietary name request under the NDA will have a 90-day PDUFA goal date.

Conclusion

The Applicant responded that they understand our preliminary concern and appreciate the courtesy call. The Applicant agrees to submit an alternative name.

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/s/

MARIA R WASILIK
05/12/2011



IND 103130
NDA 202344

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

EffRx Pharmaceuticals SA
c/o Hurley Consulting Associates Ltd.
One Main Street
Chatham, NJ 07928

ATTENTION: Susan M. Mondabaugh, PhD, FRAPS
Vice President, Regulatory Affairs

Dear Dr. Mondabaugh:

Please refer to your Investigational New Drug Application (IND), submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act and to your New Drug Application (NDA) dated December 21, 2010, received December 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Alendronate Sodium, Effervescent Tablets, 70 mg.

We also refer to your December 8, 2010, IND correspondence, received December 9, 2010, and to your March 29, 2011, NDA correspondence, received March 29, 2011, requesting review of your proposed proprietary name, Steovess. We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

(b) (4)

IND 103130
NDA 202344
Page 2

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Maria Wasilik, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Karl Stiller at (301) 796-1993.

Sincerely,

{See appended electronic signature page}

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

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/s/

CAROL A HOLQUIST
05/11/2011



NDA 202344

FILING COMMUNICATION

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

Please refer to your New Drug Application (NDA) dated December 21, 2011, received February 15, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for alendronate sodium effervescent tablets, 70mg.

We also refer to your submission dated March 31, 2011.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is December 15, 2011.

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, midcycle, 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 November 6, 2011.

During our filing review of your application, we identified the following potential review issues:

Clinical

1. Your risk/benefit discussion (M 2.5) regarding the potential for upper GI irritation of your product includes the issue of buffering of gastric acid, but does not address the role of alendronate particulate matter. Submit and discuss the evidence that your [REDACTED] (b) (4) product does not result in significant particulate matter which may be retained within the esophagus.
2. Provide a rationale for the applicability of your data to the U.S. population/practice of medicine, as discussed in *Guidance for Industry E5 - Ethnic Factors in the Acceptability of Foreign Clinical Data* (September 2006), accessible at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073120.pdf>.

Clinical Pharmacology

1. In study AE-1212-001-EM, study subjects were instructed to drink at least 100 mL of Volvic (non-sparkling water) approximately every 30 minutes from 2 hours prior to dosing to approximately 30 minutes after dosing for a total of 740 mL when taking effervescent alendronate sodium tablet or Fosamax. However, the approved Fosamax labeling instructs patients to take Fosamax with a full glass of water (6-8 ounces). Address the effect of difference in the total amount of water consumption (740 mL vs. 6-8 ounces) while taking Fosamax on the safety and efficacy of Fosamax.
2. The current proposed labeling for effervescent alendronate sodium tablet instructs patients to take each effervescent alendronate sodium tablet by dissolving it in 4 ounces of water. Address the effect of the difference in the total amount of water consumption (740 mL vs. 4 ounces) while taking effervescent alendronate sodium tablet on the bioavailability of effervescent alendronate sodium tablet.

Chemistry, Manufacturing, and Controls

1. Provide information on whether the blisters comply with 16 CFR 1700.14(a)(10) for child resistance. Refer to the US Consumer Product Safety Commission website (<http://www.cpsc.gov/businfo/dreg.html>) for more information.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

Please respond only to the above requests for information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues:

Highlights (HL)

1. HL must be in two-column format, with ½ inch margins on all sides and between columns, and in a minimum of 8-point font.
2. HL is limited in length to one-half page.

Initial U.S. Approval

1. The verbatim statement “Initial U.S. Approval” followed by the 4-digit year in which the FDA initially approved the new molecular entity (NME), new biological product, or new combination of active ingredients, must be placed immediately beneath the product title line. For alendronate sodium, the statement should read “Initial U.S. Approval 1995.”

Contraindications

1. List known hazards and not theoretical possibilities (i.e., hypersensitivity to the drug or any inactive ingredient). If the contraindication is not theoretical, describe the type and nature of the adverse reaction.

Patient Counseling Information Statement

1. Change the statement to reference the Medication Guide: “**See 17 for Patient Counseling Information and Medication Guide.**”

General Format

1. A horizontal line must separate the TOC and FPI.
2. The heading – **FULL PRESCRIBING INFORMATION** – must appear at the beginning in UPPER CASE and **bold** type.

Adverse Reactions

1. For the “Clinical Trials Experience” subsection, the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:
“Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be

directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.”

2. For the “Postmarketing Experience” subsection, the listing of post-approval adverse reactions must be separate from the listing of adverse reactions identified in clinical trials. Include the following verbatim statement with appropriate modification:

“The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.”

Patient Counseling Information

1. Must reference any FDA-approved patient labeling, including the type of patient labeling. The statement “See FDA-approved patient labeling (insert type of patient labeling).” should appear at the beginning of Section 17 for prominence. For example:

“See FDA-approved patient labeling (Medication Guide)”

In addition, we recommend the following revisions. Additions to current labeling are shown by underlined text and deletions are shown by ~~strike-through~~ text.

1. HIGHLIGHTS, ADVERSE REACTIONS:

The most common adverse reactions for alendronate sodium (incidence >3%) are

(b) (4)

2. FULL PRESCRIBING INFORMATION: CONTENTS*:
17 PATIENT COUNSELING INFORMATION

(b) (4)

3. 12.2 Pharmacodynamics, Osteoporosis in Postmenopausal Women subsection:
Unbold **Osteoporosis in Postmenopausal Women**

4. 17 PATIENT COUNSELING INFORMATION

(b) (4)

We request that you resubmit labeling that incorporates the above recommendations by May 13, 2011. The resubmitted labeling will be the basis for further labeling discussions.

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(s) 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 Karl Stiller, Regulatory Project Manager, at (301) 796-1993.

Sincerely,

{See appended electronic signature page}

George Benson, M.D.
Deputy Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

GEORGE S BENSON
04/28/2011



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202344

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for alendronate sodium effervescent tablets, 70mg.

You were notified in our letter dated December 27, 2010, that your application was not accepted for filing due to non-payment of fees. The Division has been notified that your request for small business waiver of the application fee for NDA 202344 has been granted on February 15, 2011, therefore, your application is now acceptable for review effective that date.

Unless we notify you within 60 days of the above date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on April 16, 2011, in accordance with 21 CFR 314.101(a).

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, contact Karl Stiller, Regulatory Project Manager, at (301) 796-1993.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph., M.P.A.
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MARGARET M KOBER

02/18/2011

Chief, Project Management Staff



NDA 202344

UNACCEPTABLE FOR FILING

EffRx Pharmaceuticals SA c/o Hurley Consulting Associates Ltd.
Attention: Susan M. Mondabaugh, Ph.D.
Vice President Regulatory Affairs
One Main Street
Chatham, NJ 07928

Dear Dr. Mondabaugh:

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

Name of Drug Product: alendronate sodium effervescent tablets, 70 mg.

Date of Application: December 21, 2010

Date of Receipt: December 22, 2010

Our Reference Number: NDA 202344

We have not received the appropriate user fee for this application. An application is considered incomplete and cannot be accepted for filing until all fees owed have been paid. Therefore, this application is not accepted for filing. We will not begin a review of this application's adequacy for filing until FDA has been notified that the appropriate fee has been paid. Payment should be submitted to the following address:

Food and Drug Administration
P.O. Box 70963
Charlotte, NC 28272-0963

Checks sent by a courier should be addressed to:

Wells Fargo Bank
Attn: Food and Drug Administration, Lockbox 70963
1525 West WT Harris Blvd, Room D1113-022
Charlotte, NC 28262

NOTE: Please include the User Fee I.D. Number, the Application number, and the FDA P.O. Box number (P.O. Box 70963) on the enclosed check. It would be helpful if you included the user fee cover sheet (Form FDA 3397) with your payment.

The receipt date for this submission (which begins the review for filability) will be the date the review division is notified that payment has been received by the bank.

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

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

If you wish to send payment by wire transfer, or if you have any other questions, please call Bev Friedman or Mike Jones at 301-796-3602.

If you have any questions, contact Karl Stiller, Regulatory Project Manager, at (301) 796-1993.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph., M.P.A.
Chief, Project Management Staff
Division of Reproduction and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MARGARET M KOBER
12/27/2010
Chief, Project Management Staff

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

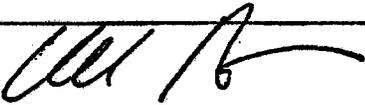
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

| | | |
|------------------------|--|--|
| Clinical Investigators | | |
| | | |
| | | |

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

| | |
|--|--------------------------------------|
| NAME Marshall Hayward, Ph.D. | TITLE Chief Scientific Officer |
| FIRM/ORGANIZATION Efferx Pharmaceuticals SA | |
| SIGNATURE  | DATE (mm/dd/yyyy) 8 December 2010 |

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

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Food and Drug Administration
Office of Chief Information Officer
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