

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203922Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 203922

SUPPL #

HFD # 170

Trade Name none

Generic Name Sodium nitrite

Applicant Name Hope Pharmaceuticals

Approval Date, If Known February 14, 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) NOTE: Per Henry Startzman in orphan products---As long as the labeling is the same/combo use only, Hope can come in under the original orphan designation, but would not get a new period of orphan exclusivity. They would get what is remaining on the Nithiodote approval.

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

YES ☐

NO ☒

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

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

d) Did the applicant request exclusivity?

YES ☐ NO ☒

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

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

YES ☐ NO ☒

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

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

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

YES ☐ NO ☒

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES ☒ NO ☐

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

#(s).

NDA# 201444

Nithiodote

NDA# 020166

Na Thiosulfate/Na Nitrite

NDA#

2. Combination product.

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

YES ☐ NO ☒

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

NDA#

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:

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

Investigation #1

YES ☐

Explain:

!

!

! NO ☐

! Explain:

Investigation #2

YES ☐

Explain:

!

!

! NO ☐

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐

NO ☐

If yes, explain:

=====

Name of person completing form: Matt Sullivan

Title: RPM

Date: February 14, 2011

Name of Office/Division Director signing form: Rigoberto Roca, MD

Title: Deputy Director

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/

MATTHEW W SULLIVAN
02/14/2012

RIGOBERTO A ROCA
02/14/2012

1.3.3 Debarment Certification

NDA 203922
Sodium Nitrite Injection

1.3.3 Debarment Certification

Hope Pharmaceuticals certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.



Craig Sherman, M.D.

December 23, 2011

Date

President

Hope Pharmaceuticals

From: Baugh, Denise
Sent: Wednesday, February 01, 2012 2:47 PM
To: Chaudhry, Danyal
Cc: Merchant, Lubna
Subject: FW: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

Hi, Danyal!

Would you mind up-loading the e-mail trail below into DARRTS for Matt Sullivan? Thanks!

Denise

From: Sullivan, Matthew
Sent: Wednesday, February 01, 2012 2:39 PM
To: Baugh, Denise
Cc: Merchant, Lubna
Subject: RE: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

Whichever is easier is fine with us. We'd just like something on final that you saw the final versions and we're ok with them.

From: Baugh, Denise
Sent: Wednesday, February 01, 2012 2:37 PM
To: Sullivan, Matthew
Cc: Merchant, Lubna
Subject: RE: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

Hi, Matt!

DMEPA does not do amendments to our reviews. We can do a memo in which case it has to go through the editing process (and approved by management) before putting it in to DARRTS. This takes longer. The alternative is to up load my comments in to DARRTS as confirmation/documentation of my assessment of these revisions. Let me know what you prefer. Denise

From: Sullivan, Matthew
Sent: Wednesday, February 01, 2012 2:26 PM
To: Baugh, Denise
Subject: RE: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

Denise –

Are you planning on entering an amendment to your review to close the loop on these cartons? I think we'd like something so that we know you concurred with the final items.

The Sponsor submitted the cartons on 1/26 to their NDAs (the same ones they emailed us earlier that day).

From: Baugh, Denise
Sent: Thursday, January 26, 2012 4:26 PM
To: Sullivan, Matthew; Merchant, Lubna
Cc: Chaudhry, Danyal; Stradley, Sara; Simone, Arthur
Subject: RE: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

These are acceptable. Thanks, Matt!
Denise

From: Sullivan, Matthew
Sent: Thursday, January 26, 2012 4:06 PM
To: Baugh, Denise; Merchant, Lubna
Cc: Chaudhry, Danyal; Stradley, Sara; Simone, Arthur
Subject: RE: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

Denise –

I've never seen cartons come back so quickly, here are the revisions based on your comments.

[\\Fdfs01\ode2\DAAAP\NDA and sNDA\NDA 203922 \(sodium nitrite Hope\)\68587-SN Box9.pdf](#)

[\\Fdfs01\ode2\DAAAP\NDA and sNDA\NDA 203923 \(sodium thiosulfate Hope\)\68587-STX Box 10.pdf](#)

From: Baugh, Denise
Sent: Thursday, January 26, 2012 12:36 PM
To: Sullivan, Matthew; Merchant, Lubna
Cc: Chaudhry, Danyal; Stradley, Sara
Subject: RE: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

Matt,

Just two comments on the revised carton labeling:

- 1) Add a dividing line between the dosing for adults and that for children on the back panel for Sodium Thiosulfate. (I noticed that the dividing line appears on the carton labeling for Sodium Nitrite, but not for Sodium Thiosulfate).
- 2) For the side panel of the carton labeling for Sodium Nitrite, add a space between the words, "personnel" and "should" in the statement "Prior to administration, emergency personnel should be instructed in the use . . . ". (The presentation of this statement will then be consistent with that for Sodium Thiosulfate).

Thanks, Matt!
Denise

From: Sullivan, Matthew
Sent: Wednesday, January 25, 2012 5:15 PM
To: Baugh, Denise; Merchant, Lubna

Cc: Chaudhry, Danyal; Stradley, Sara

Subject: RE: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

Hi Denise –

The sponsor has emailed me the revised artwork. They said that they accepted all of your recommendations.

They also submitted an updated PI, I just haven't had a change to look it over, but will do so tomorrow.

Please let me know if you need anything else on this. The official submission should be here tomorrow – I'll forward you the load notice so you know it's here.

Matt

[\\Fdsfs01\ode2\DAAAP\NDA and sNDA\NDA 203923 \(sodium thiosulfate Hope\)\Jan 25, 2012 carton\68587-STs Box 9.pdf](#)

[\\Fdsfs01\ode2\DAAAP\NDA and sNDA\NDA 203922 \(sodium nitrite Hope\)\Jan 25, 2012 carton\68587-SN Box8.pdf](#)

From: oasfda@fda.gov [mailto:oasfda@fda.gov]

Sent: Monday, January 23, 2012 5:00 PM

To: Dallas, Scott; Baugh, Denise; Brennan, Colleen; Rappaport, Bob A; CDER OSE CONSULTS; Sullivan, Matthew; CDER-DDMAC-RPM; Merchant, Lubna; Chaudhry, Danyal; Holquist, Carol A; Taylor, Kellie; Jenkins, Darrell

Subject: Finalized - NDA 203923 Labeling Review (REV-EPIPOSTMKT-06)

(b) (4)

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/s/

AZEEM D CHAUDHRY
02/01/2012

Sullivan, Matthew

From: Sullivan, Matthew
Sent: Tuesday, January 24, 2012 4:58 PM
To: 'sherman@hopepharm.com'
Subject: Container labeling comments
Attachments: Carton Labeling.pdf

Good afternoon –

Attached are our comments regarding the container labeling for NDA 203922 and 203923. Additionally, there are a couple of comments regarding the package inserts.

Thanks,
Matt

Matthew W. Sullivan, M.S.
Senior Regulatory Project Manager
Division of Anesthesia, Analgesia,
and Addiction Products
Food and Drug Administration
Phone 301-796-1245
Fax 301-796-9723
matthew.sullivan@fda.hhs.gov

A. Carton Labeling (Sodium Nitrite Injection, USP and Sodium Thiosulfate Injection, USP)

1. The Sodium Nitrite and Sodium Thiosulfate carton labeling both (b) (4) look almost identical to each other. In addition, they also look identical to the approved Nithiodote carton labeling. To avoid selection errors, (b) (4) the approved container labels such that these cartons are distinguishable from each other and from the approved Nithiodote.
2. Delete the statement (b) (4) on the back panel (under Dosing & Administration heading) and add (b) (4) in this location. Additionally, improve the prominence of this information by bolding or adding color or by other means.
3. One of the side panels is entirely (b) (4) and information is presented in thin, (b) (4) font making it difficult to read. Revise the information on the (b) (4) side panel so that it is more prominent and visible to the reader. In addition, add the statement of strength to this panel so that this information is visible on all sides of the carton labeling.
4. Add the statement ‘Use with Sodium Thiosulfate (or Nitrite) for treatment of Cyanide Poisoning’ to the principal display panel. Additionally, we recommend you box this statement.
5. Delete the statement (b) (4) which is stated in black font on the principal display panel as this information is redundant to the statement of strength already on the principal display panel. (Deletion of this statement will also allow space for recommendation #4 above).
6. Delete the statement which begins with (b) (4) as this information clutters the label and is stated in the insert labeling.
7. Increase the font size of the strength statement to increase its readability.
8. Revise the statement (b) (4) to read “Directions for Use: See Back Panel or Package Insert” to reflect both sources of information.

B. Insert Labeling

1. Sodium Thiosulfate Injection, USP (NDA 203923)
 - a. Revise the established name (b) (4) to “Sodium Thiosulfate Injection, USP” in the Highlights of Prescribing Information Section
 - b. Revise the Dosage and Administration Section located in the Full Prescribing Information Section such that the dosing information is the same as that in the Highlights of Prescribing Information Section.

- c. Revise the statement “All parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration” to “All parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit”.
- 2. Sodium Nitrite Injection, USP (NDA 203922) - See comments B1b and B1c.

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/s/

MATTHEW W SULLIVAN
01/24/2012



NDA 203922

NDA ACKNOWLEDGMENT

Hope Pharmaceuticals
Suite 125
16416 N. 92nd St.
Scottsdale, AZ 85260

Attention: Craig R. Sherman, MD
President

Dear Dr. Sherman:

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

Name of Drug Product: Sodium Nitrite injection, 30 mg/ml

Date of Application: January 10, 2012

Date of Receipt: January 10, 2012

Our Reference Number: NDA 203922

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on March 10, 2012, in accordance with 21 CFR 314.101(a).

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

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

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

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

If you have any questions, call me at (301) 796-1245.

Sincerely,

{See appended electronic signature page}

Matthew W. Sullivan, MS
Senior Regulatory Project Manager
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

MATTHEW W SULLIVAN
01/23/2012