

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-749

21-751

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**
*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

21-749

NAME OF APPLICANT / NDA HOLDER

hameln pharmaceuticals gmbh

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

TRADE NAME (OR PROPOSED TRADE NAME)

Capenten

ACTIVE INGREDIENT(S)

diethylenetriaminepentaacetic acid (DTPA)

STRENGTH(S)

200 mg/mL

DOSAGE FORM

Sterile solution for injection

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

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

1. GENERAL

a. United States Patent Number

b. Issue Date of Patent

c. Expiration Date of Patent

d. Name of Patent Owner

Address (of Patent Owner)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

1. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

2. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

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21-751

NAME OF APPLICANT / NDA HOLDER

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For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

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b. Issue Date of Patent

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d. Name of Patent Owner

Address (of Patent Owner)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

EXCLUSIVITY SUMMARY FOR NDA # 21-749 SUPPL # _____

TradeName N/A Generic Name Pentetate calcium trisodium injection _____

Applicant Name Hameln Pharmaceuticals HFD-160

Approval Date If Known _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

FDA did the finding of safety and efficacy. Orphan drug exclusivity also applies.

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 /X/ NO /___/

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

7 years _____

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

YES /___/ NO /X/

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 /X/

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 /X___/

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

NDA# _____

NDA# _____

NDA# _____

2. Combination product.

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

YES /___/ NO /X___/

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 NDA'S 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: _____

Signature
Title:

Date

Signature of Office/
Division Director

Date

Form OGD-011347 Revised 05/10/2004

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

/s/

Sally Loewke
8/10/04 02:59:34 PM

EXCLUSIVITY SUMMARY FOR NDA # 21-751 SUPPL # _____

TradeName N/A Generic Name Pentetate zinc trisodium injection

Applicant Name Hameln Pharmaceuticals HFD-160

Approval Date If Known _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

FDA did the finding of safety and efficacy. Orphan drug exclusivity also applies.

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 /X/ NO /___/

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

7 years _____

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

YES /___/ NO /X/

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 /X/

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 /X/

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

NDA# _____
NDA# _____
NDA# _____

2. Combination product.

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

YES /___/ NO /X___/

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.

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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.

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(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 /___/

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: _____

Signature

Date

Title:

Signature of Office/
Division Director

Date

Form OGD-011347 Revised 05/10/2004

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

/s/

Sally Loewke
8/10/04 03:22:54 PM



hameln pharmaceuticals gmbh
PO Box 10 08 63, 31758 Hameln, Germany
Langes Feld 13, 31789 Hameln, Germany
<http://www.hameln-pharmaceuticals.com>

22 March 2004

**NDA 21-751 – _____™
Zn-DTPA (Pentetate Zinc Trisodium injection)**

Statements of Claimed Exclusivity and Associated Certifications

Based on the Federal Register notice encouraging the submission of applications for Ca-DTPA (Pentetate Calcium Trisodium injection) and Zn-DTPA (Pentetate Zinc Trisodium injection) (source: Fed. Reg. Vol. 68, No. 178, 15 September 2003, pp. 53984-53989), and the NDA approvals for calendar years 2003 and 2004 (<http://www.fda.gov/cder/rdmt>), no other drug product containing the active moiety [diethylenetriaminepentaacetic acid (DTPA)] has been previously approved. Therefore, _____™ Zn-DTPA (Pentetate Zinc Trisodium injection) will be eligible for exclusivity as provided in 21 CFR 314.108(b)(2) upon approval.

Alternatively, if orphan drug designation is granted to the active moiety (DTPA), _____ Zn-DTPA (Pentetate Zinc Trisodium injection) will be eligible for exclusivity as provided in 21 CFR 316.31(a).

Dr. Mathias Dewald
Head of Regulatory Affairs



hameln pharmaceuticals gmbh
PO Box 10 08 63, 31758 Hameln, Germany
Langes Feld 13, 31789 Hameln, Germany
<http://www.hameln-pharmaceuticals.com>

17 March 2004

NDA 21-749 – _____ M
Ca-DTPA (Pentetate Calcium Trisodium injection)

Debarment Certification Statement

hameln pharmaceuticals gmbh, Langes Feld 13, 31789 Hameln, Germany 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.

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

Dr. Mathias Dewald
Head of Regulatory Affairs
hameln pharmaceuticals gmbh

A handwritten signature in black ink, appearing to read "H. Ribbans", written over a horizontal line.

Helen Ribbans
U.S. Agent
President
B&H Consulting Services, Inc.



hameln
pharmaceuticals

hameln pharmaceuticals gmbh
PO Box 10 08 63, 31758 Hameln, Germany
Langes Feld 13, 31789 Hameln, Germany
<http://www.hameln-pharmaceuticals.com>

17 March 2004

NDA 21-751 – _____
Zn-DTPA (Pentetate Zinc Trisodium injection)

Debarment Certification Statement

hameln pharmaceuticals gmbh, Langes Feld 13, 31789 Hameln, Germany 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.

Dr. Mathias Dewald
Head of Regulatory Affairs
hameln pharmaceuticals gmbh

Helen Ribbans
U.S. Agent
President
B&H Consulting Services, Inc.

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA #: 21-749 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: 4/6/04 Action Date: 8/11/04

HFD-160 _____ Trade and generic names/dosage form: Pentetate calcium trisodium injection

Applicant: Hameln Pharmaceutical, GmbH Therapeutic Class: 1P

Indication(s) previously approved:

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Treatment for internal contamination with plutonium, americium and curium

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

Yes: Please proceed to Section A.

X No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

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

Other: _____

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

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

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

Other: _____

Date studies are due (mm/dd/yy): _____

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. 0 _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 16 _____ Tanner Stage _____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 21-749
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

Attachment A

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

Indication #2: _____

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

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

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

Date studies are due (mm/dd/yy): _____

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA #####
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

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/s/

Patricia Stewart
8/10/04 04:52:25 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA # : 21-751 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: 4/5/04 Action Date: 8/11/04

HFD-160 _____ Trade and generic names/dosage form: Pentetate zinc trisodium injection

Applicant: Hameln Pharmaceutical, GmbH Therapeutic Class: 1P

Indication(s) previously approved:

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Treatment for internal contamination with plutonium, americium and curium

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

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

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

Other: _____

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

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. 0 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 16 Tanner Stage _____

Reason(s) for deferral:

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

Other: A PK study has been requested as a phase 4 commitment to evaluate drug absorption, distribution and elimination when delivered by the inhalation route

Date studies are due (mm/dd/yy):

- a. Protocol submission: Within 6 months of the date of final approval of this application
- b. Study start (i.e. the date the database will be ready to accept patient data, should it be necessary): Within 6 months of agreement to the protocol
- c. Final study report submission: Within 12 months of initiation of the study

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. 0 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 16 Tanner Stage _____

Comments: Only the IV route of administration has dosing information in the labeling.

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 21-749
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG

NDA 21-749
Page 3

DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

Attachment A

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

Indication #2: _____

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

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

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

Date studies are due (mm/dd/yy): _____

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA ~~###-###~~
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 10-14-03)

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/s/

Patricia Stewart
8/10/04 04:55:33 PM



hameln pharmaceuticals gmbh
PO Box 10 08 63, 31758 Hameln, Germany
Langes Feld 13, 31789 Hameln, Germany
<http://www.hameln-pharmaceuticals.com>

22 March 2004

NDA 21-749 - _____
Ca-DTPA (Pentetate Calcium Trisodium injection)

Statement under 21 CFR § 314.50 (k)
Financial Certification or Disclosure

Ca-DTPA and Zn-DTPA in sterile aqueous solution have been used under investigational new drug applications (INDs)

- IND 4041 Ca-DTPA
- IND 14,603 Zn-DTPA

held by the Radiation Emergency Assistance Center / Training Site (REAC/TS). REAC/TS is part of the Oak Ridge Associated Universities (ORAU). ORAU operates the Oak Ridge Institute for Science and Education under a contract with the Department of Energy (Project Identifier: ORAU-78-96; Project Title: Use of Ca-DTPA and Zn-DTPA for Chelation Therapy of Heavy Metals, started: 1978).

On the basis of results obtained under these INDs and from information in the published literature, the FDA announced that Ca-DTPA and Zn-DTPA, when produced under conditions specified in approved new drug applications (NDAs), can be found to be safe and effective for the treatment of internal contamination with plutonium, americium, or curium to increase the rates of elimination (source: Fed. Reg. Vol. 68, No. 178, 15 September 2003, pp. 53984-53989).

In accordance with this, hameln pharmaceuticals gmbh, as the applicant of the NDA, is referring to the above mentioned FDA announcement (source: Fed. Reg. Vol. 68, No. 178, 15 September 2003, pp. 53984-53989) and declares, that they neither contracted with one or more clinical investigators to conduct the studies nor submitted studies conducted by others under contract to the applicant.

Dr. Mathias Dewald
Head of Regulatory Affairs



hameln pharmaceuticals gmbh
PO Box 10 08 63, 31758 Hameln, Germany
Langes Feld 13, 31789 Hameln, Germany
<http://www.hameln-pharmaceuticals.com>

22 March 2004

NDA 21-751 - _____ M
Zn-DTPA (Pentetate Zinc Trisodium injection)

Statement under 21 CFR § 314.50 (k)
Financial Certification or Disclosure

Ca-DTPA and Zn-DTPA in sterile aqueous solution have been used under investigational new drug applications (INDs)

- IND 4041 Ca-DTPA
- IND 14,603 Zn-DTPA

held by the Radiation Emergency Assistance Center / Training Site (REAC/TS). REAC/TS is part of the Oak Ridge Associated Universities (ORAU). ORAU operates the Oak Ridge Institute for Science and Education under a contract with the Department of Energy (Project Identifier: ORAU-78-96; Project Title: Use of Ca-DTPA and Zn-DTPA for Chelation Therapy of Heavy Metals, started: 1978).

On the basis of results obtained under these INDs and from information in the published literature, the FDA announced that Ca-DTPA and Zn-DTPA, when produced under conditions specified in approved new drug applications (NDAs), can be found to be safe and effective for the treatment of internal contamination with plutonium, americium, or curium to increase the rates of elimination (source: Fed. Reg. Vol. 68, No. 178, 15 September 2003, pp. 53984-53989).

In accordance with this, hameln pharmaceuticals gmbh, as the applicant of the NDA, is referring to the above mentioned FDA announcement (source: Fed. Reg. Vol. 68, No. 178, 15 September 2003, pp. 53984-53989) and declares, that they neither contracted with one or more clinical investigators to conduct the studies nor submitted studies conducted by others under contract to the applicant.

A handwritten signature in black ink, appearing to read "Dewald", written over a horizontal line.

Dr. Mathias Dewald
Head of Regulatory Affairs

MEMORANDUM

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

DATE: August 11, 2004
FROM: Julie Beitz, MD
SUBJECT: Deputy Office Director Memo

NDA 21-749 Pentetate calcium trisodium injection; Hameln Pharmaceuticals GmbH
NDA 21-751 Pentetate zinc trisodium injection; Hameln Pharmaceuticals GmbH

This memo documents my concurrence with the Division of Medical Imaging and Radiopharmaceutical Drug Product's (DMIRDP) approval action for injectable Pentetate calcium trisodium (Ca-DTPA) and Pentetate zinc trisodium (Zn-DTPA) indicated for treatment of individuals with known or suspected internal contamination with plutonium, americium, or curium to increase the rates of elimination.

Civilians and military personnel may become internally contaminated with transuranium elements as a result of detonation of a radiological dispersion device (RDD or "dirty bomb"), nuclear fallout, or nuclear power/weapons processing plant accidents. Ca- and Zn-DTPA are chelators that form complexes with plutonium, americium and curium which are readily excreted in the urine.¹ The risk of radiation-induced mutagenesis increases with increasing radiation dose; preclinical studies support the use of chelators to remove transuranium elements from the circulation before they are deposited in liver and bone.

Evidence supporting the safety and effectiveness of Ca- and Zn-DTPA is derived from data collected during the treatment of 685 individuals internally contaminated with transuranium elements while employed in the nuclear processing industry in the US over a period of 42 years. This data was collected under INDs held by the Oak Ridge Institute for Science and Education's REAC/TS (Radiation Emergency Assistance Center/ Training Site). Of these 685 individuals, 646 received at least one dose of either Ca- or Zn-DTPA. Data from urine bioassays measuring radioactive elimination were available for 286 individuals. Of these, 18 had matched pre- and post-chelation therapy urine bioassay results and represent the "efficacy cases".

On September 15, 2003 (68 FR 53984), FDA published its findings of safety and effectiveness including a list of literature citations upon which these findings were based. NDA 21-749 for Ca-DTPA and NDA 21-751 for Zn-DTPA submitted by Hameln in April 2004 rely on the FDA's evaluation of the REAC/TS data and published literature, and are therefore 505(b)(2) applications. These applications included complete chemistry, manufacturing and controls information and facilities inspections were found to be satisfactory. During this cycle, the review team considered information from additional literature citations and other available clinical data and incorporated new recommendations into the product labels for Ca- and Zn-DTPA which had been published in draft on FDA's web page in September 2003.

Dosing Recommendations

Ca- and Zn-DTPA are supplied in ampoules containing 1.0 gram (2.0 mmol) in 5 mL of sterile aqueous solution and may be administered either intravenously or by nebulizer (adults only). The recommended

adult daily dose is 1.0 gram. The recommended pediatric daily dose is 14 mg/kg for those under 12 years, not to exceed 1.0 gram/day. For nebulized therapy, Ca- or Zn-DTPA should be diluted 1:1 with saline or sterile water.

A single dose of Ca-DTPA is recommended as initial therapy. If additional chelation therapy is warranted, treatment should be switched to Zn-DTPA which may be given daily. Chelation therapy should begin as soon as possible after suspected or known internal contamination and is most effective when transuranium elements are still in the circulation. Additional dosing recommendations include:

- If Ca-DTPA is not available or treatment cannot be started within the first 24 hours after internal contamination, treatment should begin with Zn-DTPA.
- If Zn-DTPA is not available, Ca-DTPA can be given for continued treatment, along with vitamin or mineral supplements that contain zinc.
- If the route of internal contamination is through inhalation alone, then nebulized therapy will suffice. If the routes of contamination are multiple (e.g., inhalation and through wounds), then intravenous chelation therapy is preferred.
- The duration of treatment depends on the level of internal contamination and the individual's response to therapy. Levels of internal contamination should be ascertained weekly during chelation therapy to determine when to terminate treatment.
- Zn-DTPA is the preferred treatment for the pregnant woman with internal contamination.

Labeling Revisions

The previously published draft product labels for Ca- and Zn-DTPA have been revised to incorporate the following recommendations:

- The Zn-DTPA label has been revised to add inhalation as a route of administration for adults.² The previously published draft label for Ca-DTPA already specified the inhalation route. Availability of Zn-DTPA by nebulizer would be of particular benefit to the pregnant woman for whom Zn-DTPA is the preferred chelator. The safety and effectiveness of Ca- or Zn-DTPA have not been established in the pediatric population for the inhalation route.
- The Ca- and Zn-DTPA labels have been revised to state that the safety and effectiveness of the intramuscular route of administration have not been established.³

² In the REAC/TS database, an efficacy case internally contaminated with plutonium received 3 doses of nebulized Zn-DTPA 1 g each, followed by 6 doses of intravenous Zn-DTPA 1 g. Urinary excretion of plutonium after the first nebulized dose of Zn-DTPA was increased by a factor of 45. No significant adverse events were reported for this individual or for 17 other adult individuals treated with a total of 99 doses of nebulized Zn-DTPA in the REAC/TS database. The effectiveness of nebulized Zn-DTPA is supported by a preclinical study in rodents contaminated with aerosolized plutonium and americium as described in Stather, J.W., Stradling, G.N., Gray, S.A., Moody, J., and Hodgson, A. (1985): Use of DTPA for increasing the rate of elimination of Plutonium-238 and Americium-241 from rodents after their inhalation as nitrates. *Human Toxicology*, 4, 573-582. See FDA Pharmacologist's memorandum dated July 30, 2004.

³ The intramuscular route was used in 8 individuals in the REAC/TS database, none of whom were efficacy cases. Three of these experienced injection site pain. In early studies of Ca-DTPA, three deaths occurred in patients with severe hemochromatosis treated with the intramuscular route. It is not known what adverse effects if any were related to the route of administration used. At this time, there are insufficient safety and effectiveness data to recommend this route.

- The Ca- and Zn-DTPA labels have been revised to clarify that the duration of therapy depends on the amount of internal radioactive contamination and individual response to therapy.⁴
- The label for Ca-DTPA has been revised to warn about safety risks in patients with severe hemochromatosis who received up to 4 times the recommended dose of Ca-DTPA by intramuscular injection.⁵ Although a causal association between these events and the drug cannot be conclusively established, the label will recommend caution in treating patients with severe hemochromatosis with Ca-DTPA.

Tradename Review

Hameln has withdrawn its proposed tradenames for Ca- and Zn-DTPA. These products will be referred to as Pentetate calcium trisodium injection and as Pentetate zinc trisodium injection in approved labeling, respectively.

Phase 4 Studies

There are two phase 4 study commitments for these products:

- In the event of a radiation emergency, longitudinal studies involving follow-up of patient treatment data forms and placement of data into a registry for periodic analyses related to drug safety issues and uses; and
- A human pharmacokinetic study in adult subjects to compare and evaluate the absorption, distribution and elimination of Ca- and Zn-DTPA via inhalation using a commonly available jet type nebulizer (FDA approved model to be selected by the sponsor) with the intravenous route. Data on dose delivered and particle size distribution obtained using the nebulizer should be provided.

Pediatric Studies

The pediatric study requirement under the Pediatric Research Equity Act (PREA) has been fulfilled for the intravenous route of administration. We are deferring submission of a pediatric study for the inhalation route of administration for ages 0 to 16 years until August 11, 2008. This deferred pediatric study is considered a required postmarketing study commitment and the status of this study shall be reported annually according to 21 CFR 314.81. This commitment is as follows:

⁴ The previously published draft labels for Ca- and Zn-DTPA recommended a minimum of 30 days of chelation therapy. In the REAC/TS database, 72% of individuals who were treated with Ca-DTPA received only one or two doses, while the remaining individuals received 3 or more doses. Among individuals treated with Zn-DTPA, 50% received one or two doses, and the remainder received 3 or more. One individual received 338 doses of Ca-DTPA 1 gram over a 6.5 year period, and another individual received 574 doses of Zn-DTPA 1 gram over a 3.5 year period. The revised labels will clarify that the duration of therapy depends on the amount of internal contamination and individual response to therapy, that is, treatment duration cannot be predicted in advance.

⁵ FDA is aware of three deaths in patients with severe hemochromatosis who received intramuscular doses of up to 4 grams of Ca-DTPA per day. One patient became comatose and died after receiving a total of 14 grams, and the other two died after 2 weeks of daily treatment. See FDA Medical Officer's memorandum dated July 29, 2004. In contrast, the literature contains a report of a patient with a less severe case of hemochromatosis who received a total of 30 grams of Ca-DTPA by intravenous injection over 12 days and experienced no adverse events. This case is described in Kemble, J.V.H. (1964): The new chelating agent Ca-DTPA in the treatment of primary haemochromatosis. *Guy's Hospital Reports*, 113, 68-73.

- A human pharmacokinetic study in pediatric subjects to compare and evaluate the absorption, distribution and elimination of Ca and Zn DTPA via inhalation using a commonly available jet type nebulizer (FDA approved model to be selected by the sponsor) with the intravenous route. Data on dose delivered and the particle size distribution obtained using the nebulizer should be provided.

Julie Beitz, MD
Deputy Director, Office of Drug Evaluation III
CDER, FDA

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/s/

Julie Beitz
8/11/04 12:36:34 PM
DIRECTOR

MEMORANDUM

Aug. 11, 2004

TO: File

FROM: Kenneth L. Hastings, Dr.P.H.

SUBJECT: NDA 21-749

I have reviewed the action package for trisodium calcium diethylenetriaminepentaacetate and concur with the pharmacology/toxicology supervisor, Dr. Adebayo Lanionu, that the product is approvable. The product label is acceptable.

Kenneth L. Hastings, Dr.P.H.

Associate Director for Pharmacology and Toxicology

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/s/

Kenneth Hastings
8/11/04 04:24:30 PM
PHARMACOLOGIST

MEMORANDUM

Aug. 11, 2004

TO: File

FROM: Kenneth L. Hastings, Dr.P.H.

SUBJECT: NDA 21-751

I have reviewed the action package for trisodium zinc diethylenetriaminepentaacetate and concur with the pharmacology/toxicology supervisor, Dr. Adebayo Laniyonu, that the product is approvable. The product label is acceptable.

Kenneth L. Hastings, Dr.P.H.

Associate Director for Pharmacology and Toxicology

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/s/

Kenneth Hastings
8/11/04 04:29:24 PM
PHARMACOLOGIST