CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-024

LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-024

Date of Submission: August 4, 1998 and August 27, 1998

Applicant's Name: Altana, Inc.

Established Name: Gentamicin Sulfate Ophthalmic Ointment, USP

Labeling Deficiencies:

1. CONTAINER: 3.5 g

   a. Front panel

      Add the net quantity 3.5 g.

   b. Back panel

      To be in accord with the USP storage recommendations add the following statement after the storage temperature range:

      Avoid exposure to excessive heat.

   c. We encourage you to revise the color or your cap to "tan". We refer you to the Guidance for Industry for container closure system used for the packaging of Human Drugs, which reserves "tan" for anti-infective products.

2. CARTON: 1 x 1

   See comments under CONTAINER.

3. INSERT

   a. General Comment

      We encourage the inclusion of "USP" following the established name in the Title and in the DESCRIPTION section.

   b. DESCRIPTION

      Revise the second paragraph to read, "...

ointment for topical ophthalmic use. Each gram contains ...".

c. DOSAGE AND ADMINISTRATION

Revise "affected eye" to read "affected eye(s)".

d. HOW SUPPLIED

Include the strength, as seen in your DESCRIPTION section. We refer you to 21 CFR 201.57(k)(1) for further guidance.

Please revise your labels and labeling, as instructed above, and submit in final print.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

_____

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23, supplement 9	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? *See FTR.	*		
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	x		
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	

Labeling (continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			x
Do any of the inactives differ in concentration for this route of administration? *The RLD contains preservatives amd the ANDA does not.	*		
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?			x
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?	x		
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. *Not listed in the RLD.	*		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			x
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. Labeling Model:

   Garamycin® (gentamicin ophthalmic ointment, USP) Ophthalmic Ointment by Schering Corporation, S-004 approved 7/29/97 and revised 4/92.

2. Patent/exclusivity: None pending.

3. The inactive ingredients listed in the DESCRIPTION section are consistent with the firm's components and composition statements.

   NOTE: The RLD contains preservatives. The ANDA does not contain preservatives.

   [Vol. B1.1, p.85]

4. Container /Closure system:

   Tube: Tin 3.5 gram with eye tip
   Cap: black tamper proof,
   [Vol.B1.3, p. 735]

5. Manufacturing facilities

   Analytical testing of raw materials and drug product, as well as stability testing: Altana Inc.
   Melville, NY 11747

   Manufacturing process for the drug product, filling and labeling: Altanta Inc.
   Hicksville, NY 11802
   [Vol.B.1.1, section 9]

6. Bioavailability/Bioequivalence: pending

7. Packaging:

   RLD - 3.5 g tube

   ANDA - 3.5 g tube

8. Storage:

   USP - Preserve in collapsible ophthalmic ointment tubes and avoid exposure to excessive heat.

   RLD - Store between 2° to 30° C (36° to 86° F)

   ANDA - Store between 2° to 30° C (36° to 86° F)

   [See comment to firm].

Date of Review: 11/13/98

Jacqueline White, Pharm.D. 1-27-99

Primary Reviewer Date

Team Leader 1/28/99

Date

cc:

ANDA: 65-024
DUP/DIVISION FILE
HFD-613/JWhite/CHoppes (no cc)
x:\new\...65024na1.1
Review

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-024

Date of Submission: September 29, 2000

Applicant's Name: Altana, Inc.

Established Name: Gentamicin Sulfate Ophthalmic Ointment, USP

Labeling Deficiencies:

INSERT

a. TITLE

You may delete the statement "Each gram contains ... gentamicin" following the TITLE.

b. PRECAUTIONS

Add the following as the last subsection of this section.

Pediatric Use

Safety and effectiveness in neonates have not been established.

Please revise your insert labeling, as instructed above, and submit final printed labeling.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

William Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? *See FTR.	*		
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	x		
Are there any other safety concerns?		x	
Labeling			

Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			x
Do any of the inactives differ in concentration for this route of administration? *The RLD contains preservatives. The ANDA does not.	*		
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?			x
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x

Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?	x		
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. *Not listed in the RLD.	*		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			x
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. Labeling Model:

   Garamycin□ (gentamicin ophthalmic ointment, USP) Ophthalmic Ointment by Schering Corporation, S-004 approved 7/29/97 [acknowledged and retained 3/30/99] and revised 9/97.

2. Patent/exclusivity: None pending.

3. The inactive ingredients listed in the DESCRIPTION section are consistent with the firm's components and composition statements.

   NOTE: The RLD contains preservatives. The ANDA does not contain preservatives.

   [Vol. B1.1, p.85]

4. Container /Closure system:

   Tube: Tin 3.5 gram with eye tip
   Cap: black tamper proof, [redacted]
   [Vol.B1.3, p. 735]

5. Manufacturing facilities

   Analytical testing of raw materials and drug product, as well as stability testing:
   Altana Inc.
   Melville, NY 11747

   Manufacturing process for the drug product, filling and labeling:
   Altanta Inc.
   Hicksville, NY 11802
   [Vol.B.1.1, section 9]

6. Bioavailability/Bioequivalence: pending

7. Packaging:

   RLD - 3.5 g tube

   ANDA - 3.5 g tube

8. Storage:

   USP - Preserve in collapsible ophthalmic ointment tubes and avoid exposure to excessive heat.

   RLD - Store between 2° to 30° C (36° to 86° F)

   ANDA - Store between 2° to 30° C (36° to 86° F)

   [See comment to firm].

9. The firm did not revise the color of their cap. They indicated that the standard cap color for ophthalmic "ointments" is black. We will not request the firm to revise the color to "tan" at this time. "Tan" is encouraged for anti-infective ophthalmic drug products.

10. The container label and carton labeling are satisfactory in FPL as of this submission. [12 of each Are in the blue/2.1 volume.

Date of Review: 11/1/2000

Jacqueline Council Pharm D — 11/9/2000

Primary Reviewer — Date

Jacqueline Council, Pharm.D.

Team Leader — 11/13/00 Date

Charles Hoppes, R.Ph.

cc:

ANDA: 65-024
DUP/DIVISION FILE
HFD-613/JCouncil/CHoppes (no cc)
V:\firmsam\Altana\ltrs&rev\65024na2.1
Review

Endorsements: HFD-613/JCouncil
HFD-613/CHoppes

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number:	65-024
Date of Submission:	June 18, 2002
Applicant's Name:	Altana, Inc.
Established Name:	Gentamicin Sulfate Ophthalmic Ointment, USP

Labeling Deficiencies:

1. CONTAINER: 3.5 g

   The side panel of your printer's proof container label is difficult to read. Improve the readability by increasing the print size and/or using darker print.

   Please note, if your final printed container labels provide improved clarity for the text printed on the side panel, you may submit twelve final printed labels for our review

Please revise your container labels, as instructed above, and submit in final print.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

William Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 25	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? *See FTR.	*		
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	x		
Are there any other safety concerns?		x	

Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			x
Do any of the inactives differ in concentration for this route of administration? *The RLD contains preservatives. The ANDA does not.	*		
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?			x
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in			x

DESCRIPTION?			
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?	x		
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. *Not listed in the RLD.	*		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			x
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

NOTE/QUESTION TO THE CHEMIST

The reference listed drug contains preservatives. Altana does not contain preservatives.
Is this acceptable?

Chemist Response: We have asked them to perform an Antimicrobial preservative effectiveness test to justify using the proposed formulation without preservatives.
[M.S.]

APPEARS THIS WAY
ON ORIGINAL

FOR THE RECORD:

1. Labeling Model:

   Garamycin® (gentamicin ophthalmic ointment, USP) Ophthalmic Ointment by Schering Corporation, S-004 approved 7/29/97 [acknowledged and retained 3/30/99] and revised 9/97.

2. Patent/exclusivity: None pending.

3. The inactive ingredients listed in the DESCRIPTION section are consistent with the firm's components and composition statements.

   NOTE: The RLD contains preservatives. The ANDA does not contain preservatives.

   [Vol. B1.1, p.85]

4. Container /Closure system:

   Tube: Tin 3.5 gram with eye tip
   Cap: black tamper proof, [redacted]
   [Vol.B1.3, p. 735]

5. Manufacturing facilities

   Analytical testing of raw materials and drug product, as well as stability testing:
   Altana Inc.
   Melville, NY 11747

   Manufacturing process for the drug product, filling and labeling:
   Altanta Inc.
   Hicksville, NY 11802
   [Vol.B.1.1, section 9]

6. Bioavailability/Bioequivalence: pending

7. Packaging:

   RLD - 3.5 g tube

   ANDA - 3.5 g tube

8. Storage:

   USP - Preserve in collapsible ophthalmic ointment tubes and avoid exposure to excessive heat.

   RLD - Store between 2° to 30° C (36° to 86° F)

   ANDA - Store between 2° to 30° C (36° to 86° F)

   [See comment to firm].

9. The firm did not revise the color of their cap. They indicated that the standard cap color for ophthalmic "ointments" is black. We will not request the firm to revise the color to "tan" at this time. "Tan" is encouraged for anti-infective ophthalmic drug products.

APPEARS THIS WAY
ON ORIGINAL

Date of Review: 7/17/02

Date of Submission: 6/18/02

Primary Reviewer
Jacqueline Council, Pharm.D.

7-31-02
Date

Acting Team Leader
Captain Lillie Golson

7/31/02
Date

cc:

ANDA: 65-024
DUP/DIVISION FILE
HFD-613/JCouncil/LGolson (no cc)
V:\firmsam\Altana\ltrs&rev\65024na3.1
Review

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-024

Date of Submission: August 7, 2002

Applicant's Name: Altana, Inc.

Established Name: Gentamicin Sulfate Ophthalmic Ointment, USP

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: 3.5 g - Satisfactory in final print as of August 7, 2002. (Vol 4.1)

Carton Labeling: Individual carton - Satisfactory in final print as of June 18, 2002. [Vol 3.1, Attachment IX]

Professional Package Insert Labeling: Satisfactory in final print as of June 18, 2002. [Code:124438#82 R3/01- Vol.3.1, Attachment IX]

Revisions needed post approval: Delete the first paragraph (Gentamicin Sulfate, USP equivalent...) on the side panel of your container label since it is redundant to the second paragraph.

BASIS OF APPROVAL:

Patent Data – 50-425

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	*None*	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data – 50-425

Code/sup	Expiration	Use Code	Description	Labeling Impact
			There is no unexpired exclusivity for this product in the Orange Book Database	

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Garamycin®
NDA Number: 50-425
NDA Drug Name: Garamycin® Gentamicin Sulfate Ophthalmic Ointment USP, 0.3% (base)
NDA Firm: Schering Corporation
Date of Approval of NDA Insert and supplement #: S-004/revised April 1992 and approved July 29, 1997
Has this been verified by the MIS system for the NDA? Yes
Was this approval based upon an OGD labeling guidance? No
Basis of Approval for the Container Labels: Garamycin® side by side
Basis of Approval for the Carton: Garamycin® side by side

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 25	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? *See FTR.	*		
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	x		
Are there any other safety concerns?		x	
Labeling			

Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			x
Do any of the inactives differ in concentration for this route of administration? *The RLD contains preservatives. The ANDA does not.	*		
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?			x
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x

Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. *Not listed in the RLD.	*		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			x
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

NOTE/QUESTION TO THE CHEMIST

The reference listed drug contains preservatives. Altana's product does not contain preservatives. Is this acceptable?

Chemist Response: We have asked them to perform an Antimicrobial preservative effectiveness test to justify using the proposed formulation without preservatives.
[M.S.]

FOR THE RECORD:

1. Labeling Model:

   Garamycin® (gentamicin ophthalmic ointment, USP) Ophthalmic Ointment by Schering Corporation, S-004 approved 7/29/97 [acknowledged and retained 3/30/99] and revised 9/97.

2. Patent/exclusivity: None pending.

3. The inactive ingredients listed in the DESCRIPTION section are consistent with the firm's components and composition statements.

NOTE: The RLD contains preservatives. The ANDA does not contain preservatives. [Vol. B1.1, p.85]

The chemist has asked the firm to perform an Antimicrobial preservative effectiveness test to justify using the proposed formulation without Preservative.

4. Container /Closure system:

Tube: Tin 3.5 gram with eye tip
Cap: black tamper proof, ———————
[Vol.B1.3, p. 735]

5. Manufacturing facilities

Analytical testing of raw materials and drug product, as well as stability testing:
Altana Inc.
Melville, NY 11747

Manufacturing process for the drug product, filling and labeling:
Altanta Inc.
Hicksville, NY 11802
[Vol.B.1.1, section 9]

6. Packaging:

RLD - 3.5 g tube

ANDA - 3.5 g tube

7. Storage:

USP - Preserve in collapsible ophthalmic ointment tubes and avoid exposure to excessive heat.

RLD - Store between 2° to 30° C (36° to 86° F)

ANDA - Store between 2° to 30° C (36° to 86° F). Avoid exposure to excessive heat.

8. The firm did not revise the color of their cap. They indicated that the standard cap color for ophthalmic "ointments" is black. We will not request the firm to revise the color to "tan" at this time. "Tan" is encouraged for anti-infective ophthalmic drug products.

Date of Review: 12/23/02

Date of Submission: 8/7/02

Michelle Dillahunt
Primary Reviewer
Michelle Dillahunt

12/23/02
Date

Ralph Vega for
Acting Team Leader
Captain Lillie Golson

1/3/03
Date

cc:

ANDA: 65-024
DUP/DIVISION FILE
HFD-613/JCouncil/LGolson (no cc)
V:\firmsam\Altana\ltrs&rev\65024ap2.l
Review

SUPERSEDES THE APPROVAL SUMMARY FOR THE SUBMISSION DATED AUGUST 7, 2002

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-024

Date of Submissions: May 7, 2003
June 12, 2003

Applicant's Name: Altana, Inc.

Established Name: Gentamicin Sulfate Ophthalmic Ointment, USP

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: 3.5 g - Satisfactory in final print as of June 12, 2003 (Vol 6.1)

Carton Labeling: Individual carton - Satisfactory in final print as of June 12, 2003. [Vol 6.1]

Professional Package Insert Labeling: Satisfactory in final print as of May 7, 2003. [Code:124438A#82 R4/03- Vol.5.4, Attachment XXI]

Revisions needed post approval:
Delete the first paragraph (Gentamicin Sulfate, USP equivalent...) on the side panel of your container label since it is redundant to the second paragraph.
Include the statement that was submitted in your previous labeling, "Avoid exposure to excessive heat" to appear following your storage recommendation in your container and insert labeling.

BASIS OF APPROVAL:

Patent Data – 64-093

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	*None*	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data – 64-093

Code/sup	Expiration	Use Code	Description	Labeling Impact
			There is no unexpired exclusivity for this product in the Orange Book Database	

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Garamycin®
NDA Number: 50-425 (now discontinued) ANDA -64-093 (RLD)
NDA Drug Name: Gentamicin Sulfate Ophthalmic Ointment USP, 0.3% (base)
NDA Firm: Akorn
Date of Approval of NDA Insert and supplement #: Approved 8/31/95
Has this been verified by the MIS system for the NDA? Yes
Was this approval based upon an OGD labeling guidance? No
Basis of Approval for the Container Labels: side by side
Basis of Approval for the Carton: side by side

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 25	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? *See FTR.	*		
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	x		
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see		x	

ASHP guidelines)			
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			x
Do any of the inactives differ in concentration for this route of administration? *The RLD contains preservatives. The ANDA does not.	*		
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?			x
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	

Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. ***Not listed in the RLD.**	*		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			x
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

NOTE/QUESTION TO THE CHEMIST

The discontinued reference listed drug contains preservatives. Altana's product does not contain preservatives.
Is this acceptable?

Chemist Response: We have asked them to perform an Antimicrobial preservative effectiveness test to justify using the proposed formulation without preservatives.
[M.S.]
From Chemist review #2
An antimicrobial preservative effectiveness test was performed using the proposed formulation without preservatives. The data submitted shows that the product as formulated is adequately preserved (pages 14-20) .

FOR THE RECORD:

1. Labeling Model:

   NDA 50-425 Garamycin Oph. Ointment is discontinued, the RLD which is an ANDA is 64-093, Gentamicin Sulfate ophthalmic ointment, USP) by Akorn, Inc.approved 8/31/95

2. Patent/exclusivity: None pending.

3. The inactive ingredients listed in the DESCRIPTION section are consistent with the firm's components and composition statements.

   NOTE: The discontinued RLD contains preservatives. The ANDA does not contain preservatives. [Vol. B1.1, p.85]

   The chemist has asked the firm to perform an Antimicrobial preservative effectiveness test to justify using the proposed formulation without Preservative.

4. Container /Closure system:

   Tube: Tin 3.5 gram with eye tip
   Cap: black tamper proof, [redacted]
   [Vol.B1.3, p. 735]

5. Manufacturing facilities

   Analytical testing of raw materials and drug product, as well as stability testing:
   Altana Inc.

Melville, NY 11747

Manufacturing process for the drug product, filling and labeling:
Altanta Inc.
Hicksville, NY 11802
[Vol.B.1.1, section 9]

6. Packaging:

RLD - 3.5 g tube

ANDA - 3.5 g tube

7. Storage:

USP - Preserve in collapsible ophthalmic ointment tubes and avoid exposure to excessive heat.

RLD - Store between 2° to 30° C (36° to 86° F)

ANDA - Store at 25° C (77 ° F); excursions permitted to 15-30 C (58° to 86° F).

8. The firm did not revise the color of their cap. They indicated that the standard cap color for ophthalmic "ointments" is black. We will not request the firm to revise the color to "tan" at this time. "Tan" is encouraged for anti-infective ophthalmic drug products.

Date of Review: 6/24/03

Date of Submissions: 5/7/03 and 6/12/03

Primary Reviewer
Michelle Dillahunt

6/26/03
Date

Team Leader
Lillie Golson

6/26/03
Date

cc:

ANDA: 65-024
DUP/DIVISION FILE
HFD-613/MDillahunt/LGolson (no cc)
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Review