

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
21-818 and 21-498/S-003

CHEMISTRY REVIEW(S)

**DIVISION OF SPECIAL PATHOGEN
AND IMMUNOLOGIC DRUG PRODUCTS**

Review of Chemistry, Manufacturing and Controls

NDA #: 21-818

DATE REVIEWED: 08-JUN-2005

CHEMISTRY REVIEW #: 1

REVIEWER: Gene W. Holbert, Ph.D.

<u>SUBMISSION:</u>	<u>DOCUMENT DATE:</u>	<u>CDER DATE:</u>	<u>ASSIGNED DATE:</u>
Original	29-MAY-2002	29-MAY-2002	04-JUN-2002
Amendment (BC)	23-OCT-2002	25-OCT-2002	29-OCT-2002
Amendment (BZ)	18-JUN-2004	22-JUN-2004	23-JUN-2004
Amendment (BZ)	25-JUN-2004	28-JUN-2004	02-JUL-2004
Amendment (AZ)	17-DEC-2004	20-DEC-2005	

The above were all submitted to NDA 21-497, Alinia (nitazoxanide) Tablets and incorporated into NDA 21-818 by reference.

NAME & ADDRESS OF SPONSOR:

Romark Laboratories, L.C.
3000 Bayport Drive, Suite 200
Tampa, FL 33607

REPRESENTATIVE:

Marc S. Ayers, President and CEO
(813) 282-8544

DRUG PRODUCT NAME:

Proprietary: Alinia
Nonproprietary: Nitazoxanide
Code Name/#: PH 5776, NTZ
Chem. Type/Ther. Class: 6P

PHARMACOLOGICAL CATEGORY: Antiprotozoal

INDICATION: Treatment of diarrhea caused by *Cryptosporidium parvum*

DOSAGE FORM/STRENGTH: Tablets/500 mg

ROUTE OF ADMINISTRATION: Oral

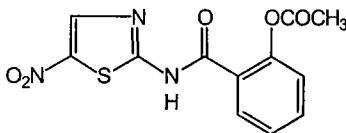
Rx/OTC: ☒ Rx ☐ OTC

SPECIAL PRODUCTS: ☐ Yes ☒ No

CHEMICAL NAME/STRUCTURAL FORMULA:

Chemical Name: 2-(Acetyloxy)-N-(5-nitro-2-thiazolyl)benzamide

Structural Formula:



Molecular Formula: C₁₂H₉N₃O₅S Molecular Weight: 307.29 CAS: 55981-090-4

SUPPORTING DOCUMENTS: The application references the following:

DMFs:

INDs: 48, 620, _____, 58,895. _____

NDAs: 21-497, 21-498, 20-871

RELATED DOCUMENTS:

COMMENTS: NDA 21-497 for Alinia (nitazoxanide) Tablets, 500 mg was approved on November 22, 2002. All of the submissions listed above were reviewed for that application. This Type 6 NDA provides for the additional indication of treatment of diarrhea caused by *Cryptosporidium parvum*. Approval of this application will result in an increase in the use of the active ingredient. Romark has therefore claimed categorical exclusion from environmental assessment under the provisions of 21 CFR 25.31 (b), increased use of the active ingredient, but the estimated concentration at the point of entry into the aqueous environment will be below 1 ppb. The sponsor is not aware of any extraordinary circumstances.

CONCLUSIONS & RECOMMENDATIONS: Adequate. From the CMC perspective, APPROVAL of this application is recommended.

Gene W. Holbert, Ph.D., Review Chemist

Concurrence:

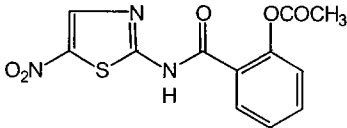
HFD-590: M. Seggel

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/s/

Gene Holbert
6/10/05 02:04:48 PM
CHEMIST

Mark Seggel
6/10/05 02:13:35 PM
CHEMIST

SUPPLEMENTAL NDA CHEMIST'S REVIEW		1. ORGANIZATION: HFD-590	2. NDA NUMBER: 21-498
3. NAME AND ADDRESS OF APPLICANT: (City and State) Romark Laboratories, L.C. 3000 Bayport Drive, Suite 200 Tampa, FL 33607-8416		4. SUBMISSION TYPE: Prior Approval	
		5. SUPPLEMENT(S):	
		NUMBER(S): SE5-003	DATE(S): 17-DEC-2004
6. NAME OF DRUG: Alina for Oral Suspension Alina for Oral Suspension		7. NONPROPRIETARY NAME: nitazoxanide	
8. SUPPLEMENT PROVIDES FOR: Addition of an indication the treatment of diarrhea caused by <i>Cryptosporidium parvum</i> in patients 12 years and older.		9. AMENDMENTS/REPORTS:	
10. PHARMACOLOGICAL CATEGORY: Antiprototzoal	11. HOW DISPENSED: ☒ Rx ☐ OTC	12. RELATED IND/NDA/DMF(S): DMFs: _____ INDs: 48, 620, _____ 58,895, _____ NDAs: 21-497, 21-498, 20-871	
13. DOSAGE FORM(S): Powder for Oral Suspension		14. POTENCY(IES): 100 mg/5 mL	
15. CHEMICAL NAME AND STRUCTURE: 2-(Acetyloxy)-N-(5-nitro-2-thiazolyl)benzamide  Molecular Formula: C ₁₂ H ₉ N ₃ O ₅ S Molecular Weight: 307.29 CAS: 55981-090-4		16. MEMORANDA:	
17. COMMENTS: This supplement was submitted to provide for the use of Alinia for Oral Suspension in treatment of diarrhea caused by <i>Cryptosporidium parvum</i> . There are no CMC changes. Romark has claimed categorical exclusion from environmental assessment under the provisions of 21 CFR 25.31(b) since approval of this application will result in increased use of the product but the estimated concentration of the drug substance at the point of entry into the aquatic environment will be below 1 ppb. Romark also states that there are no extraordinary circumstances to the best of their knowledge. Romark has proposed to eliminate the word "talc" from the Description section of the label since it appears twice. This editorial change could have been made in the annual report.			
18. CONCLUSIONS AND RECOMMENDATIONS: Approval of this supplement will have no affect on the identity, strength, quality, purity of potency of the produce. APPROVAL of this supplement is recommended.			
19. REVIEWER: Gene W. Holbert, Ph.D.		SIGNATURE: {See appended electronic signature page}	DATE COMPLETED: 09-JUN-2005
20. CONCURRENCE: Mark R. Seggel, Ph.D.		{See appended electronic signature page}	

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/s/

Gene Holbert
6/10/05 02:11:42 PM
CHEMIST

Mark Seggel
6/10/05 02:16:48 PM
CHEMIST



NDA 21-497

AliniaTM (nitazoxanide) Tablets

Romark Laboratories, L.C.

Gene W. Holbert, Ph.D.

**Division of Special Pathogen
and Immunologic Drug Products**

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Chemistry Review Data Sheet

1. NDA 21-497
2. REVIEW #2
3. REVIEW DATE: 24-JUN-2004
4. REVIEWER: Gene W. Holbert, Ph.D.
5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
NDA 20-871	26-DEC-1997
Amendment	25-FEB-1998
Amendment	03-MAR-1998
Amendment	27-APR-1998
CMC Review	18-MAY-1998
NA Letter	30-JUN-1998
NDA 21-497	28-MAY-2002
Amendment (BC)	23-OCT-2002
CMC Review	09-OCT-2003

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
NDA 21-497 (Resubmitted)	28-JAN-2004
Amendment (BZ)	18-JUN-2004
Amendment (BZ)	25-JUN-2004
Amendment (BC)	07-JUL-2004

7. NAME & ADDRESS OF APPLICANT:

Name:	Romark Laboratories, L.C.
Address:	6200 Courtney Campbell Causeway, Suite 200 Tampa, FL 33607
Representative:	Marc S. Ayers, President
Telephone:	(813) 282-8544

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Alinia™
- b) Non-Proprietary Name (USAN): Nitazoxanide
- c) Code Name/# (ONDC only): NTZ
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type: 1
 - Submission Priority: P

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Antiprotozoal

11. DOSAGE FORM: Tablets

12. STRENGTH/POTENCY: 500 mg

13. ROUTE OF ADMINISTRATION: Oral

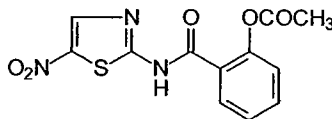
14. Rx/OTC DISPENSED: X Rx OTC15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
 SPOTS product – Form Completed

 X Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: 2-(Acetyloxy)-N-(5-nitro-2-thiazolyl)benzamide

Structural Formula:



Molecular Formula: C₁₂H₉N₃O₅S

Molecular Weight: 307.29

CAS: 55981-090-4



CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
C	II		Nitazoxanide	1	Adequate	15-SEP-2002	LOA 28-JAN-2002
	III			1	Adequate	15-SEP-2000 (D.N.Klein)	LOA 26-FEB-2002
	III			1	Adequate	27-SEP-2000 (D.N.Klein)	LOA 27-FEB-2002 Bottles found adequate
	III			1	Adequate	05-JUL-1994 (J.Fan)	LOA 26-FEB-2002 Bottles found adequate
	III			1	Adequate	06-AUG-2002 13-AUG-1993	LOA 03-APR-2002
	IV			4	N/A		LOA 30-JAN-2002
	III			1	Adequate	27-MAR-2002 (E.Chikhale)	LOA 211-JAN-2004
	III			1	Adequate	29-OCT-1997 (S.K. Kim)	LOA 26-JAN-2004
	III			1	Adequate	15-OCT-2001 (D.N. Klein)	LOA 27-JAN-2004
	III			1	Adequate	29-OCT-2003 (S.C. Pope)	LOA 09-JUN-2004

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

Chemistry Review Data Sheet

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	20-871	Nitazoxanide Tablets
NDA	21-498	Nitazoxanide Suspension
IND	48,620	<i>Cryptosporidium parvum</i> in AIDS patients
IND		
IND	58,895	NTZ suspension for Cryptosporidiosis
IND		

18. STATUS:

CONSULTS / CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES	Adequate	03-MAR-2004	
Pharm/Tox			
Biopharm	Approval	12-JUL-2004	Dakshina M. Chilukuri, Ph.D
LNC			
Methods Validation	Not required		
ODS	Minor labeling changes	28-JUN-2004	Alina R. Mahmud, R.Ph
EA	N/A		
Microbiology			

The Chemistry Review for NDA 21-497

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the chemistry, manufacturing and controls standpoint, this application may be Approved.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Alinia™ (nitazoxanide) Tablets are proposed for treatment of diarrhea caused by *Cryptosporidium parvum* and *Giardia lamblia*

_____ This product has been designated as an Orphan Drug for each of these indications since there is no alternative therapy. Alinia™ was therefore granted a priority review.

Each yellow, film-coated tablet contains 500 mg of the active ingredient, nitazoxanide, and the following excipients: maize starch, pregelatinized corn starch, hydroxypropyl methylcellulose, sucrose, sodium starch glycolate, talc, magnesium stearate, soy lecithin, polyvinyl alcohol, xanthan gum, titanium dioxide, talc, FD&C Yellow No. 10 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, and FD&C Blue No. 2 Aluminum Lake.

The active ingredient, nitazoxanide (NTZ) is a synthetic antiprotozoal agent for oral administration. The chemical name for NTZ is 2-acetyloxy-*N*-(5-nitro-2-thiazolyl)-benzamide. NTZ is a light yellow crystalline powder and is practically insoluble in water.

Alinia™ Tablets are packaged in — blister packs of 6 tablets and in HDPE bottles of 60 tablets.

Executive Summary Section

For the majority of chemistry, manufacturing and controls information regarding the drug substance, reference is made to DMF — . A majority of the information on the drug product is incorporated by cross-reference to NDA 20-871 for Alinia™ (nitazoxanide) Tablets. NDA 20-871 was submitted in December 1997 for treatment of cryptosporidial diarrhea in AIDS patients.

— This review — the current application, NDA 21-497.

B. Description of How the Drug Product is Intended to be Used

Alinia™ (nitazoxanide) Tablets are proposed for treatment of diarrhea caused by *Cryptosporidium parvum* and *Giardia lamblia* —

— Treatment of diarrhea due to *C. parvum* in patients with AIDS has not been fully studied. Alinia™ Tablets are therefore not indicated in that patient population.

This product is contraindicated in patients with known hypersensitivity to nitazoxanide.

For each of the therapeutic indications, the recommended dose in adults and adolescents 12 years of age and older is 500 mg every 12 hours for 3 days. Tablets should be taken with food.

The safety and effectiveness of this product in children younger than 12 years of age have not been studied. An application for Alinia™ Oral Suspension (NDA 21-498) for use in the pediatric population was submitted and approved on 22-NOV-2002.

Alinia™ Tablets are supplied as round, yellow film-coated tablets debossed with ALINIA on one side and 500 on the other. Each tablet contains 500 mg nitazoxanide. The tablets are packaged in white HDPE bottles, 60 tablets per bottle or in PVC blister packs of 6 tablets.

The tablets are to be stored at controlled room temperature (15-25°C, 59-77°F).

C. Basis for Approvability or Not-Approval Recommendation

The NDA submissions and the Drug Master File ultimately provided adequate information on the chemistry and manufacturing controls for the production of Alinia® Tablets. During the review, a number of issues, including the following were resolved:

- Containers used for storage of the bulk tablets prior to final packaging were not described.

Executive Summary Section

- Acceptance criteria for the drug product were modified to reflect the capabilities of the manufacturer. The proposed limits for _____ were reduced from _____ at release _____, at expiry to _____ at release _____, at expiry. The limit for Total Degradation Products was reduced from not more than _____ to not more than _____ at expiry.
- No photostability data using the current film coating had been provided.
- The original NDA 20-871 contained only 6 months of stability data for the proposed commercial formulation.

As amended, all acceptance criteria and analytical method were found adequate to ensure the identity, strength, quality, purity and potency of the drug product.

The firm had originally proposed the proprietary name "NTZ" for nitazoxanide tablets in NDA 20-871. NTZ was found to be unacceptable to the CDER Labeling and Nomenclature Committee at the time. The LNC found the name "Cryptaz" to be acceptable. Most recently, DDMAC has found the name "Cryptaz" to be objectionable

DDMAC did not object to the alternate name ' _____' Ultimately the sponsor chose the name "Alinia", to which the agency agreed.

III. Administrative

A. Reviewer's Signature

{Signed electronically in DFS}

B. Endorsement Block

Chemist Name/Date: Gene W. Holbert/
Chemistry Team Leader Name/Date: Mark R. Seggel (acting)
Project Manager Name/Date: Kristen E. Miller

C. CC Block

12 Page(s) Withheld

✓ Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

Withheld Track Number: Chemistry-

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/s/

Gene Holbert
7/9/04 10:42:24 AM
CHEMIST

Mark Seggel
7/9/04 12:53:03 PM
CHEMIST



NDA 21-497

Cryptaz (nitazoxanide) Tablets

Romark Laboratories, L.C.

Gene W. Holbert, Ph.D.

**Division of Special Pathogen
and Immunologic Drug Products**

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Chemistry Review Data Sheet

1. NDA 21-497
2. REVIEW #: 1
3. REVIEW DATE: 09-OCT-2002
4. REVIEWER: Gene W. Holbert
5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
NDA 20-871	26-DEC-1997
Amendment	25-FEB-1998
Amendment	03-MAR-1998
Amendment	27-APR-1998
CMC Review	18-MAY-1998
NA Letter	30-JUN-1998

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	28-MAY-2002
Amendment (BC)	23-OCT-2002

7. NAME & ADDRESS OF APPLICANT:

Name:	Romark Laboratories, L.C.
Address:	6200 Courtney Campbell Causeway Suite 800 Tampa, FL 33607
Representative:	Marc S. Ayers
Telephone:	(813) 282-8544



CHEMISTRY REVIEW



Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Cryptaz®
- b) Non-Proprietary Name (USAN): nitazoxanide
- c) Code Name/# (ONDC only): PH 5776, NTZ
- d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type : 1
- Submission Priority : P

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Antiprotozoal

11. DOSAGE FORM: Tablets

12. STRENGTH/POTENCY: 500 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: X Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

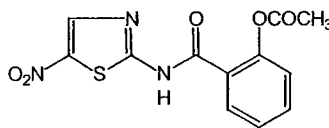
 SPOTS product – Form Completed

 X Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: 2-(Acetyloxy)-N-(5-nitro-2-thiazolyl)benzamide

Structural Formula:



Molecular Formula: C₁₂H₉N₃O₅S

Molecular Weight: 307.29

CAS: 55981-090-4



CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
/	II	/	Nitazoxanide	1	Adequate	15-SEP-2002	LOA 28-JAN-2002
	III			1	Adequate	15-SEP-2000	LOA 26-FEB-2002
	III			7	N/A		LOA 27-FEB-2002 Bottles found adequate
	III			7	N/A		LOA 26-FEB-2002 Bottles found adequate
	III			1	Adequate	06-AUG-2002 13-AUG-1993	LOA 03-APR-2002
	IV			4	N/A		LOA 30-JAN-2002

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

<u>DOCUMENT</u>	<u>APPLICATION NUMBER</u>	<u>DESCRIPTION</u>
NDA	20-871	NTZ Tablets
NDA	21-498	NTZ Suspension
IND	48,620	<i>Cryptosporidium parvum</i> in AIDs patients
IND	58,895	NTZ suspension for Cryptosporidiosis



CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. STATUS:

CONSULTS/CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES	Pending		
Pharm/Tox			
Biopharm	NLT — (Q) of the labeled amount dissolved as nitazoxanide and tizoxanide (desacetylnitazoxanide) combined at 60 minutes.		Dakshina Chilukuri
LNC			
Methods Validation			
DMETS	Does not recommend use of the name "Cryptaz"	01-NOV-2002	Tia M. Harper-Velazquez
EA	N/A		
Microbiology	N/A		
DDMAC	"Cryptaz" acceptable if approved for a Cryptosporidium indication.	11-OCT-2002	Jim Rogers

The Chemistry Review for NDA 21-497

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the chemistry, manufacturing and controls standpoint, this application may be Approved.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Cryptaz® (nitazoxanide) Tablets are proposed for treatment of diarrhea caused by Cryptosporidium parvum and Giardia lamblia

..... This product has been designated as an Orphan Drug for each of these indications since there is no alternative therapy. Cryptaz® was therefore granted a priority review.

Each yellow, film-coated tablet contains 500 mg of the active ingredient, nitazoxanide, and the following excipients: maize starch, pregelatinized corn starch, hydroxypropyl methylcellulose, sucrose, sodium starch glycolate, talc, magnesium stearate, soy lecithin, polyvinyl alcohol, xanthan gum, titanium dioxide, talc, FD&C Yellow No. 10 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, and FD&C Blue No. 2 Aluminum Lake.

The active ingredient, nitazoxanide (NTZ) is a synthetic antiprotozoal agent for oral administration. The chemical name for NTZ is 2-acetyloxy-*N*-(5-nitro-2-thiazolyl)-benzamide. NTZ is a light yellow crystalline powder and is practically insoluble in water.

For the majority of chemistry, manufacturing and controls information regarding the drug substance, reference is made to DMF _____. A majority of the information on the drug product is incorporated by cross-reference to NDA 20-871 for Cryptaz® (nitazoxanide) Tablets. NDA 20-871 was submitted in December 1997 for treatment of

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cryptosporidial diarrhea in AIDS patients.

B. Description of How the Drug Product is Intended to be Used

Cryptaz® (nitazoxanide) Tablets are proposed for treatment of diarrhea caused by *Cryptosporidium parvum* and *Giardia lamblia*

Treatment of diarrhea due to *C. parvum* in patients with AIDS has not been fully studied. Cryptaz® Tablets are therefore not indicated in that patient population.

This product is contraindicated in patients with known hypersensitivity to nitazoxanide.

For each of the therapeutic indications, the recommended dose in adults and adolescents 12 years of age and older is 500 mg every 12 hours for 3 days. Tablets should be taken with food.

The safety and effectiveness of this product in children younger than 12 years of age have not been studied. An application for Cryptaz® Oral Suspension (NDA 21-498) for use in the pediatric population has been submitted and is under active review at this time.

Cryptaz® Tablets are supplied as round, yellow film-coated tablets debossed with CRYPTAZ on one side and 500 on the other. Each tablet contains 500 mg nitazoxanide. The tablets are packaged in white HDPE bottles, 60 tablets per bottle.

The tablets are to be stored at controlled room temperature (15-25°C, 59-77°F).

C. Basis for Approvability or Not-Approval Recommendation

The NDA submissions and the Drug Mater File ultimately provided adequate information on the chemistry and manufacturing controls for the production of Cryptaz® Tablets. During the review, a number of issues, including the following were resolved:

- Containers used for storage of the bulk tablets prior to final packaging were not described.
- Acceptance criteria for the drug substance were modified to reflect the capabilities of the manufacturer. The proposed limits for desacetylnitazoxanide were reduced from — at release/ — at expiry to — at release — at expiry.
- No photostability data using the current film coating had been provided.
- NDA 20-871 contained only 6 months of data for the proposed commercial formulation.

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As amended, all acceptance criteria and analytical method were found adequate to ensure the identity, strength, quality, purity and potency of the drug product.

The firm had originally proposed the proprietary name "NTZ" for nitazoxanide tablets in NDA 20-871. NTZ was found to be unacceptable to the CDER Labeling and Nomenclature Committee at the time. The LNC found the name "Cryptaz" to be acceptable. Most recently, DDMAC has found the name "Cryptaz" to be objectionable since it suggests indications for the product such as cryptosporidium and cryptococcus. DDMAC does not object to the alternate name "

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Chemist Name/Date: Gene W. Holbert/09-OCT-2002
Chemistry Team Leader/Date: Norman R. Schmuff//
Project Manager Name/Date: Kristen Miller/

C. CC Block

21 Page(s) Withheld

✓ Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

Withheld Track Number: Chemistry-

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

/s/

Gene Holbert
11/22/02 04:21:31 PM
CHEMIST

Norman Schmuff
11/26/02 06:37:14 AM
CHEMIST