

NITAZOXANIDE - nitazoxanide tablet

ANI Pharmaceuticals, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use NITAZOXANIDE TABLETS safely and effectively. See full prescribing information for NITAZOXANIDE TABLETS.

NITAZOXANIDE tablets, for oral use

Initial U.S. Approval: 2002

INDICATIONS AND USAGE

Nitazoxanide tablet is an antiprotozoal indicated for the treatment of diarrhea caused by *Giardia lamblia* or *Cryptosporidium parvum* (1). (1)

Limitations of Use: (1)

Nitazoxanide tablet has not been shown to be effective for the treatment of diarrhea caused by *C. parvum* in HIV-infected or immunodeficient patients (1). (1)

DOSAGE AND ADMINISTRATION

- Nitazoxanide tablets should not be administered to pediatric patient 11 years of age or younger (2.1).
- Dosage for treatment of diarrhea caused by *G. lamblia* or *C. parvum* (2.1):

Age	Dosage	Duration
12 years and older	One nitazoxanide tablet (500 mg nitazoxanide) every 12 hours with food	3 days

DOSAGE FORMS AND STRENGTHS

Nitazoxanide Tablets: 500 mg (3.1) (3)

CONTRAINDICATIONS

Hypersensitivity (4.1) (4)

ADVERSE REACTIONS

The most common adverse reactions in $\geq 2\%$ of patients were abdominal pain, headache, chromaturia, and nausea (6.1). (5)

To report SUSPECTED ADVERSE REACTIONS, contact ANI Pharmaceuticals, Inc. at 1-855-204-1431 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. (5)

DRUG INTERACTIONS

Competition for binding sites may occur when administered concurrently with other highly plasma protein-bound drugs with narrow therapeutic indices. Monitor for adverse reactions (7). (6)

USE IN SPECIFIC POPULATIONS

Pediatric Patients: Safety and efficacy of ALINIA[®] for Oral Suspension in pediatric patients less than one year of age has not been studied (8.4). (7)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS & USAGE

2 DOSAGE & ADMINISTRATION

2.1 Recommended Dosage and Important Administration Instructions

3 DOSAGE FORMS & STRENGTHS

3.1 Nitazoxanide Tablets (500 mg)

4 CONTRAINDICATIONS

4.1 Hypersensitivity

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

6.2 Postmarketing Experience

7 DRUG INTERACTIONS

7.1 Highly Protein Bound Drugs with Narrow Therapeutic Indices

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Renal and Hepatic Impairment

8.7 HIV-Infected or Immunodeficient Patients

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.3 Pharmacokinetics

12.4 Microbiology

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis & Mutagenesis & Impairment Of Fertility

14 CLINICAL STUDIES

14.1 Diarrhea Caused by *G. lamblia*

14.2 Diarrhea Caused by *C. parvum*

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 Nitazoxanide Tablets (500 mg)

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS & USAGE

Diarrhea caused by *Giardia lamblia* or *Cryptosporidium parvum*:

Nitazoxanide tablets (patients 12 years and older) are indicated for the treatment of diarrhea caused by *Giardia lamblia* or *Cryptosporidium parvum*.

Limitations of Use

Nitazoxanide tablets have not been shown to be effective for the treatment of diarrhea caused by *Cryptosporidium parvum* in HIV-infected or immunodeficient patients [see *Clinical Studies (14.2)*].

2 DOSAGE & ADMINISTRATION

2.1 Recommended Dosage and Important Administration Instructions

Important Administration Instructions for Pediatric Patients 11 years of Age or Younger:

Nitazoxanide tablets should not be administered to pediatric patients 11 years of age or younger because a single tablet contains a greater amount of nitazoxanide than the recommended dosing in this pediatric age group.

Table 1. Recommended Dosage

Age	Dosage	Duration
12 years and older	One nitazoxanide tablet (500 mg nitazoxanide) taken orally every 12 hours with food.	3 days

3 DOSAGE FORMS & STRENGTHS

3.1 Nitazoxanide Tablets (500 mg)

Round, yellow, film-coated tablets debossed with 'ZNN' on one side, plain on the other side, and free from physical defects. Each tablet contains 500 mg of nitazoxanide.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

Nitazoxanide tablets and ALINIA for Oral Suspension are contraindicated in patients with a prior hypersensitivity to nitazoxanide or any other ingredient in the formulations.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of nitazoxanide was evaluated in 2177 HIV-uninfected subjects 12 months of age and older who received nitazoxanide tablets or ALINIA for Oral Suspension at the recommended dose for at least three days. In pooled controlled clinical trials involving 536 HIV-uninfected subjects treated with nitazoxanide tablets or ALINIA for Oral Suspension, the most common adverse reactions were abdominal pain, headache, chromaturia and nausea ($\geq 2\%$).

Safety data were analyzed separately for 280 HIV-uninfected subjects ≥ 12 years of age receiving nitazoxanide at the recommended dose for at least three days in 5 placebo-controlled clinical trials and for 256 HIV-uninfected subjects 1 through 11 years of age in

7 controlled clinical trials. There were no differences between the adverse reactions reported for nitazoxanide-treated subjects based upon age.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of nitazoxanide. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following is a list of adverse reactions spontaneously reported with nitazoxanide tablets which were not included in clinical trial listings:

Gastrointestinal disorders: diarrhea, gastroesophageal reflux disease

Nervous System disorders: dizziness

Respiratory, thoracic and mediastinal disorders: dyspnea

Skin and subcutaneous tissue disorders: rash, urticaria

7 DRUG INTERACTIONS

7.1 Highly Protein Bound Drugs with Narrow Therapeutic Indices

Tizoxanide (the active metabolite of nitazoxanide) is highly bound to plasma protein (>99.9%). Therefore, monitor for adverse reactions when administering nitazoxanide concurrently with other highly plasma protein-bound drugs with narrow therapeutic indices, as competition for binding sites may occur (e.g., warfarin).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data with nitazoxanide in pregnant women to inform a drug-associated risk. No teratogenicity or fetotoxicity was observed in animal reproduction studies with administration of nitazoxanide to pregnant rats and rabbits during organogenesis at exposures 30 and 2 times, respectively, the exposure at the maximum recommended human dose of 500 mg twice daily based on body surface area (BSA).

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Nitazoxanide was administered orally to pregnant rats at doses of 0, 200, 800 or 3200 mg/kg/day on gestation days 6 to 15. Nitazoxanide produced no evidence of systemic maternal toxicity when administered once daily via oral gavage to pregnant female rats at levels up to 3200 mg/kg/day during the period of organogenesis.

In rabbits, nitazoxanide was administered at doses of 0, 25, 50, or 100 mg/kg/day on gestation days 7 to 20. Oral treatment of pregnant rabbits with nitazoxanide during organogenesis resulted in minimal maternal toxicity and no external fetal anomalies.

8.2 Lactation

Risk Summary

No information regarding the presence of nitazoxanide in human milk, the effects on the breastfed infant, or the effects on milk production is available. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for nitazoxanide and any potential adverse effects on the breastfed infant from nitazoxanide or from the underlying maternal condition.

8.4 Pediatric Use

The safety and efficacy of ALINIA for Oral Suspension for the treatment of diarrhea caused by *G. lamblia* or *C. parvum* in pediatric patients 1 to 11 years of age has been established based on three (3) randomized, controlled studies with 104 pediatric subjects treated with ALINIA for Oral Suspension 100 mg/5 mL. Furthermore, the safety and efficacy of ALINIA for Oral Suspension for the treatment of diarrhea caused by *G. lamblia* or *C. parvum* in pediatric patients 12 to 17 years of age has been established based on two (2) randomized controlled studies with 44 pediatric subjects treated with ALINIA for Oral Suspension 100 mg/5 mL [see *Clinical Studies (14.1)*].

The safety and efficacy of nitazoxanide tablets for the treatment of diarrhea caused by *G. lamblia* or *C. parvum* in pediatric patients 12 to 17 years of age has been established based on three (3) randomized controlled studies with 47 pediatric subjects treated with nitazoxanide tablets 500 mg.

A single nitazoxanide tablet contains a greater amount of nitazoxanide than is recommended for use in pediatric patients 11 years or younger. [see *Dosage and Administration (2.1)*].

Safety and efficacy of ALINIA for Oral Suspension in pediatric patients less than one year of age has not been studied.

8.5 Geriatric Use

Clinical studies of nitazoxanide tablets and ALINIA for Oral Suspension did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy in

elderly patients should be considered when prescribing nitazoxanide tablets and ALINIA for Oral Suspension.

8.6 Renal and Hepatic Impairment

The pharmacokinetics of nitazoxanide in patients with compromised renal or hepatic function has not been studied.

8.7 HIV-Infected or Immunodeficient Patients

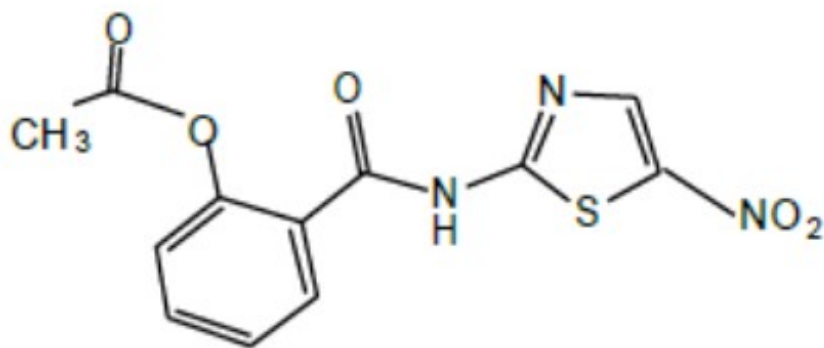
Nitazoxanide tablets and ALINIA for Oral Suspension have not been studied for the treatment of diarrhea caused by *G. lamblia* in HIV-infected or immunodeficient patients. Nitazoxanide tablets and ALINIA for Oral Suspension have not been shown to be superior to placebo for the treatment of diarrhea caused by *C. parvum* in HIV-infected or immunodeficient patients [see *Clinical Studies (14)*].

10 OVERDOSAGE

Limited information on nitazoxanide overdose is available. In the event of overdose, gastric lavage may be appropriate soon after oral administration. Patients should be observed and given symptomatic and supportive treatment. There is no specific antidote for overdose with nitazoxanide. Because nitazoxanide is highly protein bound (>99.9%), dialysis is unlikely to significantly reduce plasma concentrations of the drug.

11 DESCRIPTION

Nitazoxanide tablets contain the active ingredient, nitazoxanide, a synthetic antiprotozoal for oral administration. Nitazoxanide is a light yellow crystalline powder. It is poorly soluble in ethanol and practically insoluble in water. Chemically, nitazoxanide is 2-acetyloxy-*N*-(5-nitro-2-thiazolyl)benzamide. The molecular formula is C₁₂H₉N₃O₅S and the molecular weight is 307.3. The structural formula is:



Nitazoxanide tablets contain 500 mg of nitazoxanide and the following inactive ingredients: corn starch, sodium starch glycolate type A, sucrose, hydroxypropyl methylcellulose, talc, magnesium stearate, polyvinyl alcohol, titanium dioxide, D&C yellow #10 aluminum lake, lecithin (soy), xanthan gum, FD&C yellow #6 aluminum lake, FD&C blue #2 aluminum lake.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Nitazoxanide is an antiprotozoal [see *Microbiology (12.4)*].

12.3 Pharmacokinetics

Absorption

Single Dosing:

Following oral administration of nitazoxanide tablets or ALINIA for Oral Suspension, the parent drug, nitazoxanide, is not detected in plasma. The pharmacokinetic parameters of the metabolites, tizoxanide and tizoxanide glucuronide are shown in Tables 2 and 3 below.

Table 2. Mean (\pm SD) plasma pharmacokinetic parameters of tizoxanide and tizoxanide glucuronide following administration of a single dose of one 500 mg nitazoxanide tablet with food to subjects \geq 12 years of age.

Age	Tizoxanide			Tizoxanide Glucuronide		
	C _{max} (μ g/mL)	*T _{max} (hr)	AUC _t (μ g•hr/mL)	C _{max} (μ g/mL)	*T _{max} (hr)	AUC _t (μ g•hr/mL)
12-17 years	9.1 (6.1)	4.0 (1-4)	39.5 (24.2)	7.3 (1.9)	4.0 (2-8)	46.5 (18.2)
\geq 18 years	10.6 (2.0)	3.0 (2-4)	41.9 (6.0)	10.5 (1.4)	4.5 (4-6)	63.0 (12.3)

* T_{max} is given as a Mean (Range)

Table 3. Mean (\pm SD) plasma pharmacokinetic of tizoxanide and tizoxanide glucuronide parameter values following administration of a single dose of ALINIA for Oral Suspension with food to subjects \geq 1 year of age

Age	Dose	Tizoxanide			Tizoxanide Glucuronide		
		C _{max} (μ g/mL)	*T _{max} (hr)	AUC _{inf} (μ g•hr/mL)	C _{max} (μ g/mL)	*T _{max} (hr)	AUC _{inf} (μ g•hr/mL)
1-3 years	100 mg	3.11 (2.0)	3.5 (2-4)	11.7 (4.46)	3.64 (1.16)	4.0 (3-4)	19.0 (5.03)
4-11 years	200 mg	3.00 (0.99)	2.0 (1-4)	13.5 (3.3)	2.84 (0.97)	4.0 (2-4)	16.9 (5.00)
\geq 18 years	500 mg	5.49 (2.06)	2.5 (1-5)	30.2 (12.3)	3.21 (1.05)	4.0 (2.5-6)	22.8 (6.49)

* T_{max} is given as a Mean (Range)

Multiple dosing:

Following oral administration of a single nitazoxanide tablet every 12 hours for 7 consecutive days, there was no significant accumulation of nitazoxanide metabolites tizoxanide or tizoxanide glucuronide detected in plasma.

Bioavailability:

ALINIA for Oral Suspension is not bioequivalent to nitazoxanide tablets. The relative bioavailability of the suspension compared to the tablet was 70%.

When nitazoxanide tablets are administered with food, the AUC_∞ of tizoxanide and tizoxanide glucuronide in plasma is increased almost two-fold and the C_{max} is increased by almost 50%.

When ALINIA for Oral Suspension was administered with food, the AUC_∞ of tizoxanide and tizoxanide glucuronide increased by about 45-50% and the C_{max} increased by ≤10%.

Nitazoxanide tablets and ALINIA for Oral Suspension were administered with food in clinical trials and hence they are recommended to be administered with food [see *Dosage and Administration (2.1)*].

Distribution

In plasma, more than 99% of tizoxanide is bound to proteins.

Elimination

Metabolism

Following oral administration in humans, nitazoxanide is rapidly hydrolyzed to an active metabolite, tizoxanide (desacetyl-nitazoxanide). Tizoxanide then undergoes conjugation, primarily by glucuronidation.

Excretion

Tizoxanide is excreted in the urine, bile and feces, and tizoxanide glucuronide is excreted in urine and bile. Approximately two-thirds of the oral dose of nitazoxanide is excreted in the feces and one-third in the urine.

Specific Populations

–

Pediatric Patients

The pharmacokinetics of tizoxanide and tizoxanide glucuronide following administration of nitazoxanide tablets in pediatric patients 12-17 years of age are provided above in

Table 2. Mean (\pm SD) plasma pharmacokinetic parameters of tizoxanide and tizoxanide glucuronide following administration of a single dose of one 500 mg nitazoxanide tablet with food to subject ≥ 12 years of age. The pharmacokinetics of tizoxanide and tizoxanide glucuronide following administration of ALINIA for Oral Suspension in pediatric patients 1-11 years of age are provided above in Table 3. Mean (\pm SD) plasma pharmacokinetic of tizoxanide and tizoxanide glucuronide parameter values following administration of a single dose of ALINIA for Oral suspension with food to subjects ≥ 1 year of age.

Drug Interaction Studies

In vitro studies demonstrated that tizoxanide has no significant inhibitory effect on cytochrome P450 enzymes.

12.4 Microbiology

Mechanism of Action

The antiprotozoal activity of nitazoxanide is believed to be due to interference with the pyruvate:ferredoxin oxidoreductase (PFOR) enzyme-dependent electron transfer reaction which is essential to anaerobic energy metabolism. Studies have shown that the PFOR enzyme from *G. lamblia* directly reduces nitazoxanide by transfer of electrons in the absence of ferredoxin. The DNA-derived PFOR protein sequence of *C. parvum* appears to be similar to that of *G. lamblia*. Interference with the PFOR enzyme-dependent electron transfer reaction may not be the only pathway by which nitazoxanide exhibits antiprotozoal activity.

Resistance

A potential for development of resistance by *C. parvum* or *G. lamblia* to nitazoxanide has not been examined.

Antimicrobial Activity

Nitazoxanide and its metabolite, tizoxanide, are active *in vitro* in inhibiting the growth of (i) sporozoites and oocysts of *C. parvum* and (ii) trophozoites of *G. lamblia*.

Susceptibility Test Methods

For protozoa such as *C. parvum* and *G. lamblia*, standardized tests for use in clinical microbiology laboratories are not available.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis & Mutagenesis & Impairment Of Fertility

Carcinogenesis

Long-term carcinogenicity studies have not been conducted.

Mutagenesis

Nitazoxanide was not genotoxic in the Chinese hamster ovary (CHO) cell chromosomal aberration assay or the mouse micronucleus assay. Nitazoxanide was genotoxic in one tester strain (TA 100) in the Ames bacterial mutation assay.

Impairment of Fertility

Nitazoxanide did not adversely affect male or female fertility in the rat at 2400 mg/kg/day (approximately 20 times the clinical adult dose adjusted for body surface area).

14 CLINICAL STUDIES

14.1 Diarrhea Caused by *G. lamblia*

Diarrhea caused by *G. lamblia* in adults and adolescents 12 years of age or older:

In a double-blind, controlled trial (Study 1) conducted in Peru and Egypt in adults and adolescents with diarrhea and with one or more enteric symptoms (e.g., abdominal pain, nausea, vomiting, fever, abdominal distention, loss of appetite, flatulence) caused by *G. lamblia*, a three-day course of treatment with nitazoxanide tablets administered 500 mg twice daily was compared with a placebo tablet for 3 days. A third group of patients received open-label ALINIA for Oral Suspension administered 500 mg/25mL of suspension twice daily for 3 days. A second double-blind, controlled trial (Study 2) conducted in Egypt in adults and adolescents with diarrhea and with or without enteric symptoms (e.g., abdominal colic, abdominal tenderness, abdominal cramps, abdominal distention, fever, bloody stool) caused by *G. lamblia* compared nitazoxanide tablets administered 500 mg twice daily for 3 days to a placebo tablet. For both of these studies, clinical response was evaluated 4 to 7 days following the end of treatment. A clinical response of 'well' was defined as 'no symptoms, no watery stools and no more than 2 soft stools with no hematochezia within the past 24 hours' or 'no symptoms and no unformed stools within the past 48 hours.' The following clinical response rates were obtained:

Table 4. Adult and Adolescent Patients with Diarrhea Caused by *G. lamblia* Clinical Response Rates* 4 to 7 Days Post-therapy % (Number of Successes/Total)

	Nitazoxanide Tablets	ALINIA for Oral Suspension	Placebo Tablets
Study 1	85% (46/54) ^{¶ §}	83% (45/54) ^{¶ §}	44% (12/27)
Study 2	100% (8/8)	-	30% (3/10)

*Includes all patients randomized with *G. lamblia* as the sole pathogen. Patients failing to complete the studies were treated as failures.

[¶]Clinical response rates statistically significantly higher when compared to placebo.

§The 95% confidence interval of the difference in response rates for the tablet and suspension is (-14%, 17%).

Some patients with ‘well’ clinical responses had *G. lamblia* cysts in their stool samples 4 to 7 days following the end of treatment. The relevance of stool examination results in these patients is unknown. Patients should be managed based upon clinical response to treatment.

Diarrhea caused by *G. lamblia* in pediatric patients 1 through 11 years of age:

In a randomized, controlled trial conducted in Peru in 110 pediatric patients with diarrhea and with or without enteric symptoms (e.g., abdominal distention, right iliac fossa tenderness) caused by *G. lamblia*, a three-day course of treatment with nitazoxanide (100 mg twice daily in pediatric patients ages 24-47 months, 200 mg twice daily in pediatric patients ages 4 through 11 years) was compared to a five-day course of treatment with metronidazole (125 mg twice daily in pediatric patients ages 2 through 5 years, 250 mg twice daily in pediatric patients ages 6 through 11 years). Clinical response was evaluated 7 to 10 days following initiation of treatment with a ‘well’ response defined as ‘no symptoms, no watery stools and no more than 2 soft stools with no hematochezia within the past 24 hours’ or ‘no symptoms and no unformed stools within the past 48 hours.’ The following clinical response rates were obtained:

Table 5. Clinical Response Rates in Pediatric Patients 7 to 10 Days Following Initiation of Therapy Intent-to-Treat and Per Protocol Analyses % (Number of Successes/Total), [95% Confidence Interval]

Population	Nitazoxanide (3 days)	Metronidazole (5 days)	95% CI Diff[§]
Intent-to-treat analysis [†]	85% (47/55)	80% (44/55)	[-9%, 20%]
Per protocol analysis [¶]	90% (43/48)	83% (39/47)	[-8%, 21%]

[†]Intent-to-treat analysis includes all patients randomized with patients not completing the study treated as failures.

[¶]Per protocol analysis includes only patients who took all of their medication and completed the study. Seven patients in each treatment group missed at least one dose of medication and one in the metronidazole treatment group was lost to follow-up.

[§]95% Confidence Interval on the difference in response rates (nitazoxanide-metronidazole).

Some patients with ‘well’ clinical responses had *G. lamblia* cysts in their stool samples 4 to 7 days following the end of treatment. The relevance of stool examination results in these patients is unknown. Patients should be managed based upon clinical response to treatment.

14.2 Diarrhea Caused by *C. parvum*

Diarrhea caused by *C. parvum* in adults and adolescents 12 years of age or older:

In a double-blind, controlled trial conducted in Egypt in adults and adolescents with diarrhea and with or without enteric symptoms (e.g., abdominal pain/cramps, nausea, vomiting) caused by *C. parvum*, a three-day course of treatment with nitazoxanide tablets administered 500 mg twice daily was compared with a placebo tablet for 3 days. A third group of patients received open-label ALINIA for Oral Suspension administered 500 mg/25 mL of suspension twice daily for 3 days. Clinical response was evaluated 4 to 7 days following the end of treatment. A clinical response of 'well' was defined as 'no symptoms, no watery stools and no more than 2 soft stools within the past 24 hours' or 'no symptoms and no unformed stools within the past 48 hours.' The following clinical response rates were obtained:

Table 6. Clinical Response Rates in Adult and Adolescent Patients 4 to 7 Days Post-therapy% (Number of Successes/Total)

	Nitazoxanide Tablets	ALINIA for Oral Suspension	Placebo Tablets
Intent-to-treat analysis*	96% (27/28) ¶ §	87% (27/31)¶ §	41% (11/27)

*Includes all patients randomized with *C. parvum* as the sole pathogen. Patients failing to complete the study were treated as failures.

¶Clinical response rates statistically significantly higher when compared to placebo.

§The 95% confidence interval of the difference in response rates for the tablet and suspension is (-10%, 28%).

In a second double-blind, placebo-controlled trial of nitazoxanide tablets conducted in Egypt in adults and adolescents with diarrhea and with or without enteric symptoms (e.g., abdominal colic, abdominal cramps, epigastric pain) caused by *C. parvum* as the sole pathogen, clinical and parasitological response rates showed a similar trend to the first study. Clinical response rates, evaluated 2 to 6 days following the end of treatment, were 71% (15/21) in the nitazoxanide group and 42.9% (9/21) in the placebo group.

Some patients with 'well' clinical responses had *C. parvum* oocysts in their stool samples 4 to 7 days following the end of treatment. The relevance of stool examination results in these patients is unknown. Patients should be managed based upon clinical response to treatment.

Diarrhea caused by *C. parvum* in pediatric patients 1 through 11 years of

age:

In two double-blind, controlled trials in pediatric patients with diarrhea and with or without enteric symptoms (e.g., abdominal distention, colic, left iliac fossa tenderness) caused by *C. parvum*, a three-day course of treatment with nitazoxanide (100 mg twice daily in pediatric patients ages 12-47 months, 200 mg twice daily in pediatric patients ages 4 through 11 years) was compared with a placebo. One study was conducted in Egypt in outpatients ages 1 through 11 years with diarrhea caused by *C. parvum*. Another study was conducted in Zambia in malnourished pediatric patients admitted to the hospital with diarrhea caused by *C. parvum*. Clinical response was evaluated 3 to 7 days post-therapy with a 'well' response defined as 'no symptoms, no watery stools and no more than 2 soft stools within the past 24 hours' or 'no symptoms and no unformed stools within the past 48 hours.' The following clinical response rates were obtained:

Table 7. Clinical Response Rates in Pediatric Patients 3 to 7 Days Post-therapy Intent-to-Treat Analyses % (Number of Successes/Total)

Population	Nitazoxanide*	Placebo
Outpatient Study, age 1 - 11 years	88% (21/24)	38% (9/24)
Inpatient Study, Malnourished [¶] , age 12-35 months	56% (14/25)	23% (5/22)

*Clinical response rates statistically significantly higher compared to placebo.

[¶] 60% considered severely underweight, 19% moderately underweight, 17% mild underweight.

Some patients with 'well' clinical responses had *C. parvum* oocysts in their stool samples 3 to 7 days following the end of treatment. The relevance of stool examination results in these patients is unknown. Patients should be managed based upon clinical response to treatment.

Diarrhea caused by *C. parvum* in Acquired Immune Deficiency Syndrome (AIDS) patients:

A double-blind, placebo-controlled trial did not produce clinical cure rates that were significantly different from the placebo control when conducted in hospitalized, severely malnourished pediatric patients with acquired immune deficiency syndrome (AIDS) in Zambia. In this study, the pediatric patients received a three day course of nitazoxanide suspension (100 mg twice daily in pediatric patients ages 12-47 months, 200 mg twice daily in pediatric patients ages 4 through 11 years) and were evaluated for response four days after the end of treatment.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 Nitazoxanide Tablets (500 mg)

Nitazoxanide Tablets are round, yellow, film-coated tablets debossed with 'ZNN' on one side, plain on the other side, and free from physical defects. Each tablet contains 500 mg of nitazoxanide. The tablets are packaged in HDPE bottles as:

Bottles of 6 tablets NDC 70954-934-10

Bottles of 12 tablets NDC 70954-934-20

Bottles of 30 tablets NDC 70954-934-30

Store the tablets at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise patients and parents/caregivers of pediatric patients taking nitazoxanide tablets of the following information:

Dosage and Administration:

Nitazoxanide tablets should be taken with food.

Drug-drug Interactions:

Avoid concurrent warfarin use.

All trademarks are the property of their respective owners.

Made in India.

Neutral Code: DRUGS/AP/01/2006

Distributed by:

ANI Pharmaceuticals, Inc.

Baudette, MN 56623

Issued: 01/2025

LB4756-00

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Nitazoxanide Tablets, 500 mg

Bottles of 6 tablets NDC 70954-934-10



N 3 70954193410

NDC 70954-934-10

Nitazoxanide Tablets

500 mg

This bottle contains 6 tablets. Each tablet contains 500 mg nitazoxanide.

DOSAGE AND ADMINISTRATION: Age ≥12 years: one tablet (500 mg nitazoxanide) every 12 hours for 3 days, with food. Please see accompanying prescribing information.

STORAGE AND STABILITY: Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature]

Made in India.
Neutral Code: DRUGS/AP/01/2006
LAB-PS0218/00



Rx only
6 Tablets

Distributed by:
ANI Pharmaceuticals, Inc.
Baudette, MN 56623

LB4755-00
Issued: 01/2025

NITAZOXANIDE

nitazoxanide tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:70954-934
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
NITAZOXANIDE (UNII: SOA12P041N) (NITAZOXANIDE - UNII:SOA12P041N)	NITAZOXANIDE	500 mg

Inactive Ingredients

Ingredient Name	Strength
STARCH, CORN (UNII: O8232NY3SJ)	
LECITHIN, SOYBEAN (UNII: 1DI56QDM62)	
XANTHAN GUM (UNII: TTV12P4NEE)	
FD&C YELLOW NO. 6 ALUMINUM LAKE (UNII: GYP6Z2JR6Q)	
FD&C BLUE NO. 2 ALUMINUM LAKE (UNII: 4AQJ3LG584)	
SUCROSE (UNII: C151H8M554)	
SODIUM STARCH GLYCOLATE TYPE A (UNII: H8AV0SQX4D)	
HYPROMELLOSE 2910 (50 MPA.S) (UNII: 1IVH67816N)	
TALC (UNII: 7SEV7J4R1U)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYVINYL ALCOHOL (UNII: 532B59J990)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
D&C YELLOW NO. 10 ALUMINUM LAKE (UNII: CQ3XH3DET6)	

Product Characteristics

Color	YELLOW	Score	no score
Shape	ROUND	Size	13mm
Flavor		Imprint Code	ZNN
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:70954-934-10	6 in 1 BOTTLE; Type 0: Not a Combination Product	03/05/2025	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA214844	03/05/2025	

Labeler - ANI Pharmaceuticals, Inc. (145588013)

Revised: 3/2025

ANI Pharmaceuticals, Inc.