Nitazoxanide

**CAS Number**: 55981-09-4  
**Molecular Weight**: 307.28 g/mol  
**Molecular Formula**: C_{12}H_{9}N_{3}O_{5}S  
**Systematic (IUPAC)**: 2-[(5-nitro-1,3-thiazol-2-yl)carbamoyl]phenyl acetate

**Type**: small molecule
**Description**
Nitazoxanide, also known by the brand name Alinia, is a synthetic nitrothiazolyl-salicylamide derivative and an anti/protozoal agent. It is approved for treatment of infectious diarrhea caused by Cryptosporidium parvum and Giardia lamblia in patients 1 year of age and older. Following oral administration it is rapidly hydrolyzed to its active metabolite, tizoxanide, which is 99% protein bound. Peak concentrations are observed 1–4 hours after administration. It is excreted in the urine, bile and feces. Untoward effects include abdominal pain, vomiting and diarrhea.

**Categories**
Antiparasitic Agents

**Taxonomy**

**Kingdom** : Organic

**Classes**
Phenylacetates
Benzamides

**Substructures**
Carboxylic Acids and Derivatives
Acetates
Oxoazaniniums
Phenols and Derivatives
Amino Ketones
Phenylacetates
Ethers
Indication: For the treatment of diarrhea in adults and children caused by the protozoa Giardia lamblia and for the treatment of diarrhea in children caused by the protozoa Cryptosporidium parvum.

Pharmacodynamics: Nitazoxanide is an antifolate containing the pyrrolopyrimidine-based nucleus that exerts its antineoplastic activity by disrupting folate-dependent metabolic processes essential for cell replication. In vitro studies have shown that nitazoxanide inhibits thymidylate synthase (TS), dihydrofolate reductase (DHFR), and glycinamide ribonucleotide formyltransferase (GARFT), all folate-dependent enzymes involved in the de novo biosynthesis of thymidine and purine nucleotides. Nitazoxanide is transported into cells by both the reduced folate carrier and membrane folate binding protein transport systems. Once in the cell, nitazoxanide is converted to polyglutamate forms by the enzyme folylpolyglutamate synthetase. The polyglutamate forms are retained in
cells and are inhibitors of TS and GARFT. Polyglutamation is a time- and concentration-dependent process that occurs in tumor cells and, to a lesser extent, in normal tissues. Polyglutamated metabolites have an increased intracellular half-life resulting in prolonged drug action in malignant cells.

**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 Giardia lamblia directly reduces nitazoxanide by transfer of electrons in the absence of ferredoxin. The DNA-derived PFOR protein sequence of Cryptosporidium parvum appears to be similar to that of Giardia lamblia. Interference with the PFOR enzyme-dependent electron transfer reaction may not be the only pathway by which nitazoxanide exhibits antipROTOZOAL activity.

**Absorption**: The relative bioavailability of the suspension compared to the tablet was 70%. When administered with food the AUC and Cmax increased by two-fold and 50%, respectively, for the tablet and 45 to 50% and ≤ 10%, respectively, for the oral suspension.

**Protein binding**: Very High (greater than 99%), bound to proteins. Binding is not affected by degree of renal impairment.
**Metabolism**: Rapidly hydrolyzed to an active metabolite, tizoxanide (desacetyl-nitazoxanide), followed by conjugation, primarily by glucuronidation to tizoxanide glucuronide.

**Route of elimination**: 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.

**Half life**: 3.5 hours in patients with normal renal function

**Toxicity**: In acute studies in rodents and dogs, the oral LD$_{50}$ was higher than 10,000 mg/kg. Single oral doses of up to 4000 mg nitazoxanide have been administered to healthy adult volunteers without significant adverse effects.

**Affected organisms**: Protozoa

**Uses**
This medication is used to treat diarrhea due to certain intestinal parasitic infections (i.e., Cryptosporidium parvum and Giardia lamblia).

**How To Use?**
Take this medication by mouth every 12 hours for 3 days with food, or as directed by your doctor. Children less than 11 years of age should not take these tablets. Instead, they should take nitazoxanide
Antibiotics work best when the amount of medicine in your body is kept at a constant level. Therefore, take this drug at evenly spaced intervals. Continue to take this medication until the full-prescribed amount is finished even if symptoms disappear after a few doses. Stopping this medication too early may allow the parasites to continue to grow, which may result in a relapse of the infection. Inform your doctor if your condition worsens or does not improve.

**Drug Interactions**

Your healthcare professionals (e.g., doctor or pharmacist) may already be aware of any possible drug interactions and may be monitoring you for it. Do not start, stop or change the dosage of any medicine before checking with them first. Before using this medication, tell the doctor or pharmacist of all prescription and nonprescription products you may use. Keep a list of all your medications with you, and share the list with your doctor and pharmacist.

**Why is this medication prescribed?**

Nitazoxanide is used to treat diarrhea in children and adults caused by the protozoa Cryptosporidium or Giardia. Protozoa are suspected as the cause when diarrhea lasts more than 7 days. Nitazoxanide is in a class of medications called antipROTOzoal agents. It works by stopping the growth of certain protozoa that cause diarrhea.
How should this medicine be used?
Nitazoxanide comes as a tablet and a suspension (liquid) to take by mouth. It is usually taken with food every 12 hours for 3 days. Take nitazoxanide at around the same times every day. Follow the directions on your prescription label carefully, and ask your doctor or pharmacist to explain any part you do not understand. Take nitazoxanide exactly as directed. Do not take more or less of it or take it more often than prescribed by your doctor.

Shake the suspension well before each use to mix the medication evenly.

Other uses for this medicine
This medication may be prescribed for other uses; ask your doctor or pharmacist for more information.

What special precautions should I follow?
Before taking nitazoxanide,
tell your doctor and pharmacist if you are allergic to nitazoxanide or any other medications.
tell your doctor and pharmacist what prescription and nonprescription medications, vitamins, nutritional supplements, and herbal products you are taking or plan to take. Be sure to mention any of the following: anticoagulants ('blood thinners') such as warfarin (Coumadin). Your doctor may need to change the doses of your medications or monitor you carefully for side effects.
tell your doctor if you have or have ever had human immunodeficiency virus (HIV), problems with the immune system, or liver or kidney disease.
tell your doctor if you are pregnant, plan to become pregnant, or are breast-feeding. If you become pregnant while taking nitazoxanide, call your doctor.

**What special dietary instructions should I follow?**
To prevent dehydration caused by diarrhea, make sure you or your child gets enough to drink. Take small, frequent sips of water, fruit juice, sports drinks, or broth.

**What should I do if I forget a dose?**
Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

**What side effects can this medication cause?**
Nitazoxanide may cause side effects. Tell your doctor if any of these symptoms are severe or do not go away:
- stomach pain
- headache
- upset stomach
- vomiting
- discolored urine

Some side effects can be serious. If you experience any of these symptoms, call your doctor immediately:
- skin rash
- itching

Nitazoxanide may cause other side effects. Call your doctor if you have any unusual problems while taking this medication.
What storage conditions are needed for this medicine?
Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom). Throw away any medication that is outdated or no longer needed. Throw away any unused nitazoxanide suspension after 7 days. Talk to your pharmacist about the proper disposal of your medication.

What other information should I know?
Keep all appointments with your doctor.
Patients with diabetes should know that there are 1.48 grams of sucrose in each teaspoon of nitazoxanide suspension.

Do not let anyone else take your medication. Your prescription is probably not refillable. If you still have diarrhea after you finish the nitazoxanide, call your doctor.

It is important for you to keep a written list of all of the prescription and nonprescription (over-the-counter) medicines you are taking, as well as any products such as vitamins, minerals, or other dietary supplements. You should bring this list with you each time you visit a doctor or if you are admitted to a hospital. It is also important information to carry with you in case of emergencies.
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