Pyrazinamide

CAS Number : 98-96-4
Molecular Formula : C₅H₅N₃O
Molecular Weight : 123.11 g/mol
Systematic (IUPAC) : pyrazine-2-carboxamide

Type : small molecule
**Description**
A pyrazine that is used therapeutically as an antitubercular agent.

**Categories**
Antitubercular Agents

**Taxonomy**

**Kingdom**: Organic

**Classes**
Pyrazines

**Substructures**
Amino Ketones
Carbamates and Derivatives
Pyrazines
Heterocyclic compounds
Aromatic compounds
Carboxamides and Derivatives
Imines
Carboxylic Acids and Derivatives

**Pharmacology**

**Indication**: For the initial treatment of active tuberculosis in adults and children when combined with other antituberculous agents.
**Pharmacodynamics**: Pyrazinamide kills or stops the growth of certain bacteria that cause tuberculosis (TB). It is used with other drugs to treat tuberculosis. It is a highly specific agent and is active only against Mycobacterium tuberculosis. In vitro and in vivo, the drug is active only at a slightly acid pH. Pyrazinamide gets activated to Pyrazinoic acid in the bacilli where it interferes with fatty acid synthase FAS I. This interferes with the bacterium’s ability to synthesize new fatty acids, required for growth and replication.

**Mechanism of action**: Pyrazinamide is an important sterilizing prodrug that shortens tuberculosis (TB) therapy. However, the mechanism of action of pyrazinamide is poorly understood because of its unusual properties. In literature it has been written that the pyrazinoic acid (POA), the active moiety of pyrazinamide, disrupted membrane energetics and inhibited membrane transport function at acid pH in Mycobacterium tuberculosis. The antimycobacterial activity appears to partly depend on conversion of the drug to POA. Susceptible strains of M. tuberculosis produce pyrazinamidase, an enzyme that deaminates pyrazinamide to POA, and the in vitro susceptibility of a given strain of the organism appears to correspond to its pyrazinamidase activity. Experimental evidence suggests that pyrazinamide diffuses into M. tuberculosis in a passive manner, is converted into POA by pyrazinamidase, and because of an inefficient efflux system, accumulates in huge amounts in the bacterial cytoplasm. The accumulation of POA lowers the intracellular pH to a suboptimal level that is likely to inactivate a vital target enzyme such as fatty acid
synthase. Recent studies (2007) demonstrated that pyrazinamide and its analogs inhibit the activity of purified FAS I.

Absorption: Rapidly and well absorbed from the gastrointestinal tract.

Protein binding: ~10% (bound to plasma proteins)

Metabolism: Hepatic.

Route of elimination: Approximately 70% of an oral dose is excreted in the urine, mainly by glomerular filtration within 24 hours

Half life: 9-10 hours (normal conditions)

Toxicity: Side effects include liver injury, arthralgias, anorexia, nausea and vomiting, dysuria, malaise and fever, sideroblastic anemia, adverse effects on the blood clotting mechanism or vascular integrity, and hypersensitivity reactions such as urticaria, pruritus and skin rashes.

Affected organisms: Mycobacterium tuberculosis

Uses
Pyrazinamide is used with other medications to treat tuberculosis (TB). It is an antibiotic and works by stopping the growth of bacteria. This antibiotic treats only bacterial infections. It will not work for viral
infections (such as common cold, flu). Unnecessary use or misuse of any antibiotic can lead to its decreased effectiveness.

**How To use?**

Take this medication by mouth with or without food, usually once daily or twice weekly, or as directed by your doctor. Dosage is based on your age, weight, medical condition, and response to treatment. 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. If you are taking this medication daily, take it at the same time each day. If you are taking this medication on a weekly schedule, take it on the same days of the week and at the same time each day. Mark the days on the calendar when you need to take the medication. Continue to take this medication (and other TB medications) until the full prescribed amount is finished, even if symptoms disappear. Stopping the medication too early or skipping doses may allow the bacteria to continue to grow, which may result in a return of the infection and cause the infection to be more difficult to treat (resistant). Tell your doctor if your condition persists or worsens.

**Drug Interactions**

The effects of some drugs can change if you take other drugs or herbal products at the same time. This can increase your risk for serious side effects or may cause your medications not to work correctly. These drug interactions are possible, but do not always occur. Your doctor or pharmacist can often prevent or manage interactions by changing how you use your medications.
or by close monitoring. To help your doctor and pharmacist give you the best care, be sure to tell your doctor and pharmacist about all the products you use (including prescription drugs, nonprescription drugs, and herbal products) before starting treatment with this product. While using this product, do not start, stop, or change the dosage of any other medicines you are using without your doctor's approval. This medication may interfere with certain laboratory tests (including urine ketone tests), possibly causing false test results. Make sure laboratory personnel and all your doctors know you use this drug. This document does not contain all possible interactions. Keep a list of all the products you use. Share this list with your doctor and pharmacist to lessen your risk for serious medication problems.

**Why is this medication prescribed?**
Pyrazinamide kills or stops the growth of certain bacteria that cause tuberculosis (TB). It is used with other drugs to treat tuberculosis. This medication is sometimes prescribed for other uses; ask your doctor or pharmacist for more information.

**How should this medicine be used?**
Pyrazinamide comes as a tablet to take by mouth. It usually is taken once a day (at the same time each day) or in larger doses twice a week. Pyrazinamide may be taken with or without food. Follow the directions on your prescription label carefully, and ask your pharmacist or doctor to explain any part you do not understand. Take pyrazinamide exactly as directed. Do not take more or less of it or take it more often than prescribed by your doctor.
What special precautions should I follow?
Before taking pyrazinamide,
tell your doctor and pharmacist if you are allergic to pyrazinamide, niacin, ethionamide (Trecator-SC), or any other drugs.
tell your doctor and pharmacist what prescription and nonprescription medications you are taking, especially allopurinol (Zyloprim), colchicine and/or probenecid (Col-Probenecid, Benemid), ethionamide (Trecator-SC), and vitamins.
tell your doctor if you have or have ever had gout, liver or kidney disease, or diabetes.
tell your doctor if you are pregnant, plan to become pregnant, or are breast-feeding. If you become pregnant while taking pyrazinamide, call your doctor.
plan to avoid unnecessary or prolonged exposure to sunlight and to wear protective clothing, sunglasses, and sunscreen. Pyrazinamide may make your skin sensitive to sunlight.

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 take only your regularly scheduled dose. Do not take a double dose to make up for a missed one.

What side effects can this medication cause?
Pyrazinamide may cause side effects. Tell your doctor if any of these symptoms are severe or do not go away:
  - upset stomach
  - fatigue
If you experience any of the following symptoms, call your doctor immediately:
  - skin rash
  - fever
  - vomiting
  - loss of appetite
  - yellowing of the skin or eyes
  - darkened urine
  - pain and swelling in the joints
  - unusual bleeding or bruising
  - difficult urination

**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. Talk to your pharmacist about the proper disposal of your medication.

**What other information should I know?**
Keep all appointments with your doctor and the laboratory. Your doctor will order certain lab tests to check your response to pyrazinamide.
If you have diabetes, pyrazinamide may interfere with urine ketone tests. If you use urine ketone tests, check with your doctor about using other types of tests while taking pyrazinamide.
Do not let anyone else take your medication. Ask your pharmacist any questions you have about refilling your prescription.
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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