PRESCRIBING INFORMATION
INCLUDING PATIENT MEDICATION INFORMATION

[Pr]ISOTAMINE®

Isoniazid, USP
100 mg and 300 mg Tablets
10 mg/mL Syrup
Powder

Antituberculosis Agent

Bausch Health, Canada Inc.
2150 St-Elzear Blvd. West
Laval, Quebec
H7L 4A8

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Control No.: 245927

PRESCRIBING INFORMATION

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ACTION

Isoniazid may be bacteriostatic or bactericidal in action, depending on the concentration of the drug attained at the site of infection and the susceptibility of the infecting organism. The exact mechanism of action of isoniazid has not been fully elucidated, but several mechanisms including interference with metabolism of bacterial proteins, nucleic acids, carbohydrates, and lipids have been proposed. One of the principal actions of the drug appears to be inhibition of mycolic acid synthesis in susceptible bacteria which results in loss of acid-fastness and disruption of the bacterial cell wall. Isoniazid is active against susceptible bacteria only when they are undergoing cell division. Susceptible bacteria may undergo 1 or 2 divisions before multiplication is arrested.

Spectrum
Isoniazid is a highly specific agent and is active only against organisms of the genus Mycobacterium. Isoniazid is active *in vitro* and *in vivo* against M. tuberculosis, M. bovis, and some strains of M. kansasii. *In vitro*, the minimum inhibitory concentration (MIC) for most susceptible mycobacteria is 0.02-0.2 mcg/mL in Lowenstein-Jensen media.

CLINICAL PHARMACOLOGY

Absorption
Isoniazid is readily absorbed from the GI tract. When given with food, the extent of absorption and peak plasma concentrations of the drug may be reduced. Following oral application of the drug, peak plasma concentrations are attained within 1-2 hours. Plasma concentrations of the drug in rapid isoniazid inactivators are 20-50 % of those in slow isoniazid inactivators.

Distribution
Isoniazid is distributed into all body tissues and fluids (including cerebrospinal fluid, pleural and ascitic fluids, skin, sputum, saliva, lungs, muscle, and caseous tissue). The drug concentrations found in the cerebrospinal fluid are reported to be 90-100 % of concurrent plasma concentrations. Isoniazid is not substantially bound to plasma proteins (0-10 %). Isoniazid readily crosses the placenta. Isoniazid is distributed into milk in concentrations approximately equal to maternal concentrations.

Biotransformation
Biotransformation of isoniazid occurs mainly in the liver. Isoniazid is acetylated by N-acetyl transferase to N-acetylisoniazid; it is the biotransformed to isonicotinic acid and monoacetylhydrazine. Monoacetylhydrazine is associated with hepatotoxicity via formation of a reactive intermediate metabolite when N-hydroxylated by the cytochrome P-450 mixed oxidase system. The rate of acetylation is genetically determined; slow acetylators are characterized by a relative lack of hepatic N-acetyl transferase.

Half-life
Adults, including elderly patients:

Fast acetylators
0.5 to 1.6 hours.

Slow acetylators
2 to 5 hours.

Acute and chronic liver disease
May be prolonged to 6.7 hrs vs 3.2 hrs in controls.

Children (age 1.5 to 15 years)
2.3 to 4.9 hours.

Neonates
7.8 and 19.8 hours found in 2 newborns who received isoniazid transplacentally. The long half-life may be due to the limited acetylation capacity of neonates.

Peak serum concentrations
3 to 7 mcg per mL after a single 300 mg oral dose.

Time to peak serum concentrations
1 to 2 hours.

Elimination
The plasma half-life of isoniazid in patients with normal renal and hepatic function ranges from 1-4 hours, depending on the rate of metabolism. In patients with severely impaired renal or hepatic function, the plasma half-life may be prolonged.

The rate of isoniazid acetylation does not appear to alter efficacy when the drug is administered daily or 2 or 3 times weekly; however, a relationship between rapid inactivation and poor therapeutic response has been noted in once-weekly intermittent regimens.

In adults with normal renal function, approximately 75-96 % of a 5 mg/kg oral dose of isoniazid is excreted in urine within 24 hours as unchanged drug and metabolites. Small amounts of the drug are also excreted in saliva, sputum and feces. Isoniazid is removed by hemodialysis or peritoneal dialysis.

INDICATIONS AND CLINICAL USE

Treatment of Mycobacterial Infections
Isoniazid is used in conjunction with at least one other antituberculosis agent in the treatment of clinical tuberculosis. Isoniazid is also used in conjunction with other antituberculosis agents in the treatment of diseases caused by other mycobacteria.

Prevention of Tuberculosis
- household members and other close contacts of individuals with recently diagnosed clinical tuberculosis.
- individuals with a significant reaction to the standard Mantoux tuberculin skin test and with findings on chest radiograph consistent with nonprogressive tuberculosis in whom there are neither positive bacteriologic findings nor a history of adequate chemotherapy.
- newly infected individuals with a tuberculin skin test conversion within the last 2 years.
- individuals with a significant reaction to the standard Mantoux tuberculin skin test in special clinical situations, including those who are receiving prolonged corticosteroid or immunosuppressive therapy, have hematologic and reticuloendothelial diseases such as leukemia or Hodgkin's disease, or have diabetes mellitus, end-stage renal disease or silicosis. Individuals with clinical situations associated with substantial, rapid weight loss or chronic undernutrition, including intestinal bypass surgery for obesity, the postgastrectomy state, chronic peptic ulcer disease or malabsorption syndromes, or carcinomas of the oropharynx and upper GI tract that prevent adequate nutrition, should also receive isoniazid preventive therapy if they have a significant reaction to the standard Mantoux tuberculin skin test.
- individuals with known or suspected human immunodeficiency virus infection.
- other individuals with a significant reaction to the standard Mantouxtuberculin skin test. Preventive therapy is indicated for individuals with a significant reaction who are younger than 35 years of age, even when none of the risk factors listed above is present.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of isoniazid and other antibacterial drugs, isoniazid should be used only to treat infections that are proven or strongly suspected to be caused by bacteria.

CONTRAINDICATIONS

Isoniazid is contraindicated in patients with chronic or acute liver disease or a history of previous isoniazid-associated hepatic injury and should be discontinued if serum aminotransferase concentrations are more than 3 times higher than the upper limit of the normal range.
Isoniazid is also contraindicated in patients with a history of severe adverse reactions to the drug, including severe hypersensitivity reactions or drug fever, chills, and arthritis.

PRECAUTIONS

Susceptibility / Resistance

Development of Drug Resistant Bacteria
Prescribing isoniazid in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of resistant organisms.

Natural and acquired resistance to isoniazid have been demonstrated *in vitro* and *in vivo* in strains of M. tuberculosis. *In vitro*, resistance to isoniazid develops in a stepwise manner. The mechanism of resistance may be related to failure of the drug to penetrate or be taken up by the resistant bacteria. Resistant strains of initially susceptible bacteria develop rapidly if isoniazid is used alone in the treatment of clinical tuberculosis; however, development of resistance does not appear to be a major problem when the drug is used alone in preventive therapy. When isoniazid is combined with other antituberculosis agents in the treatment, of clinical tuberculosis, emergence of resistant strains may be delayed or prevented. There is no evidence of cross-resistance between isoniazid and other antituberculosis agents currently available.

Potential for Microbial Overgrowth
The use of isoniazid may promote the selection of non-susceptible organisms. Should superinfection occur during therapy, appropriate measures should be taken.

Liver function tests should be performed periodically in patients receiving isoniazid. In addition, patients should be questioned monthly for signs and symptoms of liver disease and should be instructed to report to their physician any of the prodromal symptoms of hepatitis (e.g., fatigue, weakness, malaise, nausea, vomiting, anorexia).

Isoniazid should be used with caution in daily users of alcohol and patients with chronic liver disease or severe renal impairment. Minor dosage adjustments may be necessary in patients with severe renal impairment.

Periodic ophthalmologic examinations should be performed in patients who develop visual symptoms while receiving the drug.

When isoniazid is used in patients who are malnourished or predisposed to neuropathy (e.g., diabetes, alcoholics), pyridoxine should generally be administered concomitantly.

ADVERSE REACTIONS

Nervous System Effects
Peripheral neuritis, usually preceded by paresthesia of the feet and hands, is the most common adverse effect of isoniazid and occurs most frequently in malnourished patients and those predisposed to neuritis (e.g., alcoholics, diabetics). Rarely, other nervous system side effects have also occurred including seizures, toxic encephalopathy, muscle twitching, ataxia, stupor, tinnitus, euphoria, memory impairment, separation of ideas and reality, loss of self-control, dizziness, and toxic psychosis. Neurotoxic effects may be prevented or relieved by the administration of 10-50 mg of pyridoxine hydrochloride daily during isoniazid therapy. In addition, optic neuritis and

atrophy have been reported with isoniazid.

Hepatic Effects
Mild hepatic dysfunction (mild and transient increases in serum SGOT, SGPT and bilirubin concentrations, has occurred in approx. 10-20 % of patients receiving isoniazid, usually during the first 4-6 months of therapy. In most cases, enzyme concentrations return to pre-treatment values despite continuation of isoniazid, but progressive liver dysfunction, bilirubinuria, jaundice, and severe and sometimes fatal hepatitis have occurred rarely. If symptoms of hepatitis or signs suggestive of hepatic damage occur during isoniazid therapy, the drug should be discontinued promptly.

Sensitivity Reactions
Hypersensitivity reactions include fever, skin eruptions (morbilliform, maculopapular, purpuric, exfoliative), lymphadenopathy, vasculitis, and, rarely, hypotension, usually 3-7 weeks following initiation of therapy. At the first sign of hypersensitivity reaction, all drugs should be discontinued. If isoniazid is reinstituted, the drug should be restarted in small and gradually increasing doses only after symptoms have cleared. If there is any indication of recurrence of hypersensitivity, isoniazid should be discontinued immediately.

Hematologic Effects
Adverse hematologic effects include agranulocytosis, eosinophilia, thrombocytopenia, methemoglobinemia, and hemolytic, sideroblastic, or aplastic anemia.

Other Adverse Effects
Reported have been in addition; nausea, vomiting, epigastric distress, dryness of the mouth, pyridoxine deficiency, pellagra, hyperglycemia, metabolic acidosis, and urinary retention and gynecomastia in males. A systemic lupus erythematosus-like syndrome and a rheumatic syndrome with arthralgia have also occurred.

DRUG INTERACTIONS

The following drug interactions and/or related problems have been reported:

Note*:* combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Acetaminophen*:* potential of increased hepatotoxicity and, possibly, nephrotoxicity.

Adrenocorticoids, Glucocorticoids*:* increased hepatic metabolism and/or excretion of isoniazid, leading to decreased plasma concentrations and effectiveness of isoniazid, especially in rapid acetylators.

Alcohol*:* concurrent daily intake of alcohol may result in increased incidence of isoniazid-induced hepatotoxicity and increased metabolism of isoniazid.

Alfentanil*:* chronic preoperative or perioperative use of isoniazid, a hepatic enzyme inhibitor, may decrease the plasma clearance and prolong the duration of action of alfentanil.

Antacids*:* antacids may delay and decrease absorption and serum concentrations of orally administered isoniazid.

Anticoagulants*:* may result in increased anticoagulant effect because of the inhibition of enzymatic metabolism of anticoagulants.

Benzodiazepines*:* isoniazid may decrease the hepatic metabolism of benzodiazepines.

Carbamazepine: serum carbamazepine levels and toxicity may be increased by isoniazid.

Cheese (Swiss, Cheshire) or Fish (tuna, skipjack Sardinella)*:* redness or itching of skin, hot feeling, rapid or pounding heartbeat, seating, chills or clammy feeling, headache, light-headedness due to the inhibition of plasma monoamine oxidase and diamine oxidase by isoniazid.

Cycloserine: increased incidence of central nervous system effects such as dizziness or drowsiness may occur.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms

Symptoms of overdosage usually occur within 30 minutes to 3 hours following ingestion of the drug. Overdosage of isoniazid has produced nausea, vomiting, dizziness, slurred speech, blurred vision, and visual hallucinations, including bright colours and strange designs. After marked overdosage, respiratory distress and CNS depression, progressing rapidly from stupor to coma, severe intractable seizures, metabolic acidosis, acetonuria, and hyperglycemia have occurred. If untreated or treated inadequately, isoniazid overdosage may be fatal. Isoniazid-induced seizures are thought to be associated with decreased g-aminobutyric acid (GABA) concentrations in the CNS, possibly resulting from inhibition by isoniazid of brain pyridoxal-5-phosphate activity.

Treatment

In the management of isoniazid overdosage, an airway should be secured, and adequate respiratory exchange established immediately. Seizures may be controlled with IV administration of diazepam or short-acting barbiturates and a dosage of pyridoxine hydrochloride equal to the amount of isoniazid ingested. Generally, 1-4 g of pyridoxine hydrochloride is given IV followed by 1 g IM every 30 minutes until the entire dose has been given. If seizures are controlled and overdosage is recent, within the last 2-3 hours, the stomach should be emptied by gastric lavage. Blood gases, serum electrolytes, glucose, and BUN determinations should be performed. Blood

should be typed and cross matched in case hemodialysis is required. Intravenous administration of sodium bicarbonate should be considered to control metabolic acidosis and repeated as needed; dosage should be adjusted on the basis of laboratory test results. Pyridoxine has also had a beneficial effect in correcting acidosis in some patients, possibly by controlling seizures and resulting lactic acidosis. Pyridoxine has been effective in treating isoniazid-induced seizures as well as other mental status changes associated with isoniazid overdosage. In several patients who remained comatose following initial treatment of seizures with diazepam and pyridoxine, administration of an additional 3- to 5 g dose of pyridoxine hydrochloride after 36-42 hours of coma resulted in complete awakening within 30 minutes. The fact that administration of high doses of pyridoxine can result in adverse neurologic effects should be considered whenever the drug is used in the treatment of isoniazid-induced seizures and/or coma.

Forced osmotic diuresis should be initiated as soon as possible following isoniazid overdosage to increase renal clearance of the drug and should be continued several hours after clinical improvement to ensure complete clearance of the drug and prevent relapse. Fluid intake and output should be monitored. In severe cases, hemodialysis or, if hemodialysis is not available, peritoneal dialysis should be used in conjunction with forced diuresis. In addition, measures should be taken to protect against hypoxia, hypotension, and aspiration pneumonia.

DOSAGE AND ADMINISTRATION

Isoniazid is administered orally either as a tablet or syrup.

Treatment of Tuberculosis
In the treatment of clinical tuberculosis and other mycobacterial diseases, isoniazid should not be given alone. Therapy should be continued long enough to prevent relapse.

The **usual adult dosage** of isoniazid for the treatment of tuberculosis is 5-10 mg/kg bodyweight once daily up to a maximum of 300 mg daily.

Children and infants tolerate larger doses of isoniazid than do adults and may be given 10-20 mg/kg of bodyweight once daily, depending on the severity of the disease. The maximum dosage for children is 300-500 mg daily.

When isoniazid is used in combination with rifampin in children, limiting isoniazid dosage to 10 mg/kg and rifampin dosage to 15 mg/kg daily may minimize the risk of hepatotoxicity. When isoniazid is used in combination with other antituberculosis drugs and the drugs are administered twice weekly, the usual adult dosage is 15 mg/kg (up to 900 mg) twice weekly and the usual dosage for children is 20-40 mg/kg (up to 900 mg) twice weekly.

Prevention of Tuberculosis
For tuberculosis preventive therapy, isoniazid usually is given alone. Preventive therapy generally should be continued for 6-12 months. The **usual adult dosage** of isoniazid for preventive therapy is 300 mg once daily.

Children and infants receive for preventive therapy isoniazid in a dosage of 10-15 mg/kg (up to 300 mg) once daily.

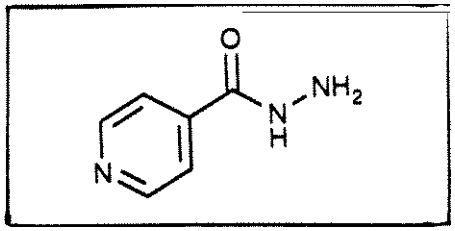
PHARMACEUTICAL INFORMATION

Drug Substance

Isoniazid, USP
(1) 4-Pyridinecarboxylic acid
(2) Isonicotinic acid hydrazide

Empirical Formula: $C_6H_7N_30$

Structural Formula:



Molecular Weight: 137.14 g/mol

Physicochemical Properties

Description: Isoniazid is a synthetic, isonicotinic acid-derivative antituberculosis agent. The drug occurs as colourless or white crystals or as a white, crystalline powder.

Solubility: Solubility of approximately 125 mg/mL in water and 20 mg/mL in alcohol at 25° C.

Stability
Isoniazid preparations should be protected from light, air, and excessive heat. Isoniazid tablets should be stored in well-closed, light-resistant containers at controlled room temperature (15 - 30° C).

ISOTAMINE Syrup: 5 mg: When a dose less than or not a multiple of 5 ml is prescribed, the syrup may be diluted with water.

Syrup must not be used as diluent as isoniazid is unstable in the presence of sugars. When stored in filled unopened containers at a temperature not exceeding 25° C, the syrup is expected to retain its potency for 1 year. When dispensed, each container should be filled, and the contents should represent not more than 1 month's supply.

Composition

ISOTAMINE tablets contain:
- Isoniazid, USP
- Microcrystalline Cellulose, NF
- Magnesium stearate, NF
- Colloidal Silicon Dioxide, NF

ISOTAMINE syrup contains:
- Isoniazid, USP
- Methylparaben, NF
- Propylparaben, NF
- Citric Acid, USP
- Sodium citrate, USP
- Glycerine, USP
- Artificial and Natural Strawberry Flavor

ISOTAMINE powder contains:
- Isoniazid, USP

AVAILABILITY

ISOTAMINE Tablets: Each white, scored, compressed tablets contain isoniazid USP 100 mg (imprinted ICN I22). Bottles of 100 and 1000 tablets.

ISOTAMINE Tablets: Each white, scored, compressed tablets contain isoniazid USP 300 mg (imprinted ICN I22). Bottles of 100 and 1000 tablets.

ISOTAMINE Syrup: Each 5 mL of clear, strawberry flavoured syrup contains: isoniazid USP 50 mg. Bottles of 500 mL

ISOTAMINE Powder: Each bottle contains: 500 g powder of isoniazid USP.

MICROBIOLOGY

***In Vitro* Activity**
Isoniazid is both tuberculostatic and tuberculocidal *in vitro*; the minimal tuberculostatic limit is 0.025 to 0.05 mcg/mL. The drug does not produce immediate inhibition of growth of M. tuberculosis, regardless of the concentration to which the organisms are exposed, the bacteria undergo one or two division before multiplication is inhibited. The bactericidal effects of isoniazid are exerted only against actively growing tubercle bacilli. Resting organisms resume normal multiplication when removed from contact with the drug. Isoniazid readily penetrates

cells and is effective against intracellularly located bacilli as well as in culture media. Isoniazid is not effective on the atypical mycobacteria.

***In Vitro* Resistance**
Static or growing cultures of M. tuberculosis contain about 60 % isoniazid-sensitive and 40 % isoniazid-resistant organisms at a given time. As multiplication progresses, and if the generation time for the culture is 24 hours, almost all the cells become susceptible to the drug over this period. If growth does not take place, a change toward a predominance of sensitive organisms does not develop.

Repeated subculture of tubercle bacilli in increasing concentration of isoniazid yields strains that are insensitive to large concentrations of the drug. Cross resistance between isoniazid and aminosalicylic acid or streptomycin does not occur.

***In Vivo* Activity**
Isoniazid is effective in the treatment of experimental tuberculosis in animals. Control of induced infection in guinea pigs is achieved with doses as low as 1 mg per day. Treated animals reveal no gross and only minimal microscopic evidence of the disease. Infections produced with tubercle bacilli resistant to aminosalicylic acid and streptomycin are effectively controlled by isoniazid.

***In Vivo* Resistance**
Treatment with isoniazid leads to large production of resistant cell populations which are initially small in the lesions of patients with tuberculosis. However, there exists considerable subject variation in the time of their appearance. Strains of M. tuberculosis that become resistant in this fashion in man are non-pathogenic or possess less invasive capacity in guinea pigs than do the parent sensitive bacteria. However, they remain pathogenic for humans. Isoniazid-insensitive tubercle bacilli isolated from patients with active infection who have never received this drug are highly pathogenic for guinea pigs, and the response to treatment with isoniazid is significantly reduced.

PHARMACOLOGY

Isoniazid is readily absorbed when administered either orally or parenterally. Peak plasma concentrations develop 1 to 2 hours after oral ingestion and fall to about 50 % or less in 6 hours. The administration of 8 mg/kg to children produces plasma levels of at least 1.6 mg/mL (0.2 to 3.2 mg/mL) in 97 % of children at 6 hours after treatment. In some individuals, tuberculostatic levels are still detectable in the blood as long as 24 hours after a single oral dose of 3 mg/kg, however, in many the quantity of circulating drug is well below that required to inhibit the organisms. Pyridoxine does not lower plasma levels of isoniazid. The simultaneous administration of aminosalicylic acid produces higher concentrations of free active isoniazid in the blood by reducing the degree of acetylation.

Isoniazid diffuses readily into all body fluids and cells and is present, in varying concentrations in all organs of humans. The drug is detectable in significant quantities in pleural and ascitic fluids, saliva and feces. Substantial levels are present in the cerebrospinal fluid of individuals

with normal meninges and in those with tuberculous meningitis. Isoniazid penetrates well into caseous material. The concentration of the agent is initially higher in the plasma and muscle than in the infected tissue, but the latter retains the drug for a long time in quantities well above those required for bacteriostasis. Skin contains large amounts of isoniazid and acts as a storage depot.

From 50 % to 79 % of a dose of isoniazid is excreted in the urine in 24 hours. Part of the drug is present in the urine in the unchanged form, the percentage varies from one individual to another. Although the main excretion products in man are acetylisoniazid and isonicotinic acid, small quantities of an isonicotinic acid conjugate, probably isonicotinyl glycine, one or more isonicotinyl hydrazones. and traces of N-methylisoniazid are also detectable in the urine. Patients may be divided into two distinct groups on the basis of the manner in which they metabolize isoniazid. In one group, all the drug is present in the urine as free isoniazid and its hydrazones, acetylisoniazid and isonicotinic acid; in the other, these compounds represent 38 % to 84 % of a dose of the agent and the quantity of free isoniazid is greater and that of acetylisoniazid is lower than in the first group. Individuals tend to maintain a constant metabolic pattern for isoniazid, and this is unrelated to the quantity administered. The incidence of peripheral neuritis appears to be higher in patients in whom urinary levels of acetylisoniazid are low and those of free isoniazid are high. Although the acetyl derivative of isoniazid is about 1/10 as toxic, it is less than 1/100 as tuberculostatic as the parent compound.

The rate of acetylation of isoniazid appears to be under genetic control. Acetylation produces at two rates, "slow" and "rapid". Plasma concentrations of the drug in a large group of individuals 6 hours after an oral dose show a bimodal distribution curve. The rate of acetylation is not influenced by sex or age but appears to be conditioned by race; it tends to be slowest in Blacks and Caucasians, most rapid in Eskimos and intermediate in Orientals. The incidence of " slow acetylators" among Americans is 44 to 54 % while in the more northern races it ranges from 7 to 27 %.

Six hours after oral administration of 4 mg/kg of isoniazid to individuals who acetylate the drug slowly, plasma concentrations are higher than 0.8 mcg/mL, while in rapid acetylators they are 0.2 mcg/mL or less. Blood levels in the latter group at 6 hours are about 50 % of peak values. In general, the concentration of active isoniazid in the circulation of rapid acetylators is about one fifth to one half of that present in persons who acetylate the drug slowly. Patients who inactivate isoniazid at a slow rate tend to develop polyneuritis more often and to experience a high frequency and more rapid reversal of infectiousness than do those who acetylate the drug rapidly.

There appears to be no relation between the development of isoniazid resistance in tubercle bacilli and the inactivator phenotype.

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READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

[Pr]ISOTAMINE®

Isoniazid, USP
100 mg and 300 mg Tablets
10 mg/mL Syrup
Powder

Read this carefully before you start taking **ISOTAMINE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ISOTAMINE.**

What is ISOTAMINE used for?

ISOTAMINE is used in adults, children and infants:

- together with other anti-tuberculosis medicines to treat tuberculosis infections.
- alone, to protect against tuberculosis infection.

Antibacterial drugs like ISOTAMINE treat only bacterial infections. They do not treat viral infections.

How does ISOTAMINE work?

ISOTAMINE contains isoniazid, an antibiotic that kills the bacteria that causes tuberculosis.

What are the ingredients in ISOTAMINE?

Medicinal ingredients: Isoniazid

Non-medicinal ingredients:
Syrup: Artificial and Natural Strawberry Flavor, Citric Acid USP, Glycerine USP, Methylparaben NF, Propylparaben, NF, Sodium Citrate USP
Tablets: Colloidal Silicon Dioxide NF, Magnesium Stearate NF, Microcrystalline Cellulose NF.

ISOTAMINE comes in the following dosage forms:

Tablets: 300 mg
Syrup: 50 mg/5 mL

Do not use ISOTAMINE if you:

- are allergic to isoniazid or to any of the other ingredients in ISOTAMINE or the materials of the container.
- have liver disease.
- have a history of liver injury caused by ISOTAMINE or another similar medicine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ISOTAMINE. Talk about any health conditions or problems you may have, including if you:

- have kidney problems
- have liver problems
- are pregnant or plan to become pregnant
- are breast-feeding or plan to breast-feed
- drink alcohol or suffer from alcoholism
- suffer from seizure or fits
- have HIV
- have diabetes
- are underweight or malnourished
- have numbness and/or tingling of arms or legs (peripheral neuropathy)

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ISOTAMINE

- Anti-Seizure medicines such as carbamazepine, primidone or phenytoin
- Aluminum hydroxide gel, an antacid used to treat heartburn, and other antacids
- Other antibiotics used to treat tuberculosis such as cycloserine and rifampin
- Disulfiram used to treat alcoholism
- Ketoconazole used to treat fungal infections
- Acetaminophen used to treat pain and fever
- Alfentanil used to control pain
- Corticosteroids used to treat inflammation
- Benzodiazepines used to treat anxiety and insomnia
- Diazepam used to treat anxiety and other mental health problems
- Blood thinners used to prevent clots
- Theophyllines used to treat breathing problems
- Cheese (Swiss, Cheshire)
- Fish (Tuna, Skipjack, Sardinella**)**
- Alcohol

How to take ISOTAMINE

- ISOTAMINE tablets & syrup should be taken at regular times, preferably after meals.
- Although you may feel better early in treatment, ISOTAMINE should be used exactly as directed.
- Do not stop taking ISOTAMINE without talking to your healthcare professional.
- Misuse or overuse of ISOTAMINE could lead to the growth of bacteria that will not be killed by ISOTAMINE (resistance). This means that ISOTAMINE may not work for you in the future
- Do not share your medicine.

Usual dose:

Treatment of Tuberculosis Infection (together with other anti-tuberculosis medicines)

Adult
Your healthcare professional will tell you how much ISOTAMINE to take based on your weight up to a maximum of 300 mg daily.

Children and Infants
Your healthcare professional will tell you how much ISOTAMINE to give your child based on their weight up to a maximum of 300-500 mg daily.

To Protect Against Tuberculosis Infection

Adults
300 mg once a day.

Children and Infants
Your healthcare professional will tell you how much ISOTAMINE to give your child based on their weight up to a maximum of 300 mg daily.

Treatment can continue for 6 to 12 months.

Overdose:

If you think you have taken too much ISOTAMINE, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Symptoms of an overdose may include:
- nausea
- vomiting
- dizziness
- slurred speech
- blurred vision
- visual hallucinations (including bright colors and strange designs)

Overdose can lead to coma and seizures.

Missed Dose:
If you missed a dose of ISOTAMINE, take it as soon as you remember.

What are possible side effects from using ISOTAMINE?
These are not all the possible side effects you may feel when taking ISOTAMINE. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- Nausea
- Vomiting
- Stomach upset and/or pain
- Dry mouth
- Enlarged breast tissue in men
- Muscle twitching
- Ringing in the ears
- Dizziness

ISOTAMINE can cause abnormal blood test results. Your healthcare professional will decide when to perform blood tests and will interpret the results.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Peripheral Neuropathy: numbness and/or tingling in the hands and feet		✓	
Liver Problems that Can Lead to Death: fatigue, weakness, loss of appetite, stomach pain, nausea, vomiting, yellowing of the skin or eyes, dark urine			✓
Eye Problems: loss of vision in one, or both eyes, eye pain that is worse when you move your eye, not seeing colours correctly			✓
Toxic Psychosis: mood changes (anxiety and/or depression), trouble sleeping, nausea, vomiting, hallucinations (hearing or seeing things that aren't there), seizures			✓
Toxic Encephalopathy: memory loss, personality changes, irritability, depression, trouble concentrating, involuntary movements, fatigue, arm weakness, seizures			✓
Allergic Reaction: rash, hives, swelling of the face, lips, tongue or throat, difficult breathing or swallowing, swollen lymph nodes, fever			✓
Seizures or fits			✓
Decreased Platelets: bruising, bleeding, fatigue and weakness		✓	
Anemia: fatigue, loss of energy, weakness,		✓	

shortness of breath			
Increased Blood Sugar: frequent urination, thirst, and hunger	✓		
Systemic Lupus Erythematosus-Like Syndrome: joint pain, muscle pain, fatigue, rash, fever, swollen lymph nodes		✓	
Urinary Retention (in males): inability to urinate, passing very little urine		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store at 15 to 30°C.
- Store in a well-closed, light-resistant container.
- Keep out of reach and sight of children.

If you want more information about ISOTAMINE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this consumer medication information by visiting the Health Canada website; (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html) or by calling 1-800-361-4261.

This leaflet was prepared by Bausch Health, Canada Inc.

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