



Isoniazid (INH) for Latent TB Infection (LTBI) Treatment



NOTE: It is imperative to rule out active TB disease in all persons prior to initiating treatment for LTBI

Is the regimen effective?

Nine months of Isoniazid is a regimen that has been historically used for the treatment of LTBI. Clinical studies of this regimen have indicated it can be ~95% effective in preventing progression to active TB with full compliance in immunocompetent subjects. However, due to poor compliance and low rates of completion, newer short-course regimens of INH/rifapentine and rifampin have much higher rates of completion and may be more appropriate for patients with no contraindications to these newer regimens.

What is the dose and regimen of INH for LTBI?

Duration	Age
9 months daily	<u>Children</u> - 10-15 mg/kg per day up to 300 mg/day (270 doses)
9 months daily	<u>Adults</u> - 5mg/kg daily (Not to exceed 300 mg/day) (270 doses)
6 months daily	<u>Children</u> –Not recommended
6 months daily	<u>Immunocompetent Adults</u> - 5 mg/kg not to exceed 300 mg/day
6 months / 9 months biweekly	<u>Adults</u> – 15 mg/dose not to exceed 900 mg/dose (Given 2 times/ week by DOT) <u>Children</u> – Not recommended

Are there situations when INH should not be used?

- Patients with known allergies to INH
- Contacts to persons with INH-resistant TB
- Other regimens are preferred for patients with liver disease or who are being administered other hepatotoxic drugs.
- There may be an increased risk of INH induced hepatotoxicity in pregnant and postpartum women. Consider postponing treatment with INH until 3 months postpartum unless the patient is at high risk for progression to active TB disease (e.g., recent TB infection, HIV positive).

What are the adverse effects of INH?

- Ten to 20% of patients taking INH experience asymptomatic LFT elevation that resolves with discontinuation of the drug.
 - INH should be discontinued when LFTs are 3 times the upper limits of normal (ULN) if the patient has symptoms of drug induced hepatitis (e.g., anorexia, fatigue, abdominal pain, jaundice) and should be discontinued if LFTs are 5 times ULN without symptoms.
 - Significant hepatotoxicity occurs very rarely in those <20 years of age, but occur with increased incidence with advancing age, liver disease, during the post-partum period, in persons with pre-existing liver disease, regular alcohol use, or taking other hepatotoxic medications.
 - Cases of fatal hepatitis have been associated with continued administration of INH after the onset of clinical hepatitis symptoms.
- Dizziness, headaches, fatigue, seizures, and peripheral neuropathy occur rarely
- Vitamin B6 (Pyridoxine) supplementation can decrease odds of peripheral neuropathy in persons who are pregnant or breast feeding, or who have HIV, renal failure, alcoholism, diabetes, or underlying peripheral neuropathy. B6 should be given to exclusively breastfed infants on INH.
- Neutropenia (very rare)

Are there drug-drug interactions with INH?

- INH can increase the blood level of phenytoin, carbamazepine and some benzodiazepines.
- Refer to product insert or other drug interaction resource for full list of interactions.



What type of monitoring is needed for INH treatment?

- Monthly interview and brief physical examination to identify treatment-associated adverse events
- Baseline hepatic chemistry is recommended for patients with specific conditions.
 - HIV infection
 - Liver disorders
 - In the immediate (within 3 months) postpartum period
 - Regular alcohol use
 - Consider also for older persons and those taking medications for chronic medical conditions
- If baseline hepatic chemistry testing is abnormal, continue with at least monthly testing and consider viral hepatitis testing.
- See “Evaluation of patients with a positive test for latent TB infection” for more information.

What is completion of treatment?

- 270 doses taken within a 12 month period or 180 doses taken within a 9 month period is considered adequate treatment.

Resources

California Department of Public Health Tuberculosis Control Branch (TBCB) website:

<http://www.cdph.ca.gov/tbcb>

California TB Controllers Association website:

<http://www.ctca.org/>

Centers for Disease Control and Prevention Division of Tuberculosis Elimination website:

<http://www.cdc.gov/tb/>

Curry International Tuberculosis Center Warmline Consultation Service, available at:

<http://www.currytbcenter.ucsf.edu/>

(877) 390-6682

American Academy of Pediatrics, Red Book Online, Tuberculosis:

<https://redbook.solutions.aap.org/chapter.aspx?sectionid=189640207&bookid=2205>

Abbreviations

AFB= acid-fast bacilli BCG= Bacillus Calmette-Guérin

CXR= chest x-ray DOT= directly observed therapy

IGRA=interferon gamma release assay LTBI= latent TB infection

MDR =multiple drug resistant NAAT= nucleic acid amplification testing

SAT= self-administered therapy TST= tuberculin skin test

