

Isoniazid (INH) for the Treatment of TB Infection

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

Is the regimen effective?

INH has been historically used as first line treatment for TB infection. Studies indicate it is ~90% effective in preventing TB disease with full compliance in immunocompetent subjects. However, due to poor compliance and low rates of completion with this regimen, newer short course regimens of isoniazid + rifapentine or only rifampin have much higher completion rates

What are the advantages of this regimen?

- There are significantly less drug-drug interactions with the INH regimen compared with the 12-dose INH + rifapentine or rifampin regimens, both of which contain rifamycins.

Who should be considered for treatment with INH for TB infection?

- HIV-infected persons receiving certain combinations of antiretroviral drugs (ARVs) that are contraindicated with rifamycins (e.g., elvitegravir, cobicistat, tenofovir alafenamide)
- Other situations where potent drug interactions with rifamycins could prove difficult to manage (e.g., transplant drugs)
- Individuals with prior adverse events or hypersensitivity to rifamycins.

Who is NOT recommended for treatment with INH?

- Contacts to persons with INH-resistant organisms
- Those with decompensated liver disease or individuals who are being administered other hepatotoxic drugs
- Hepatotoxicity has been observed during the postpartum period and is not recommended within three months of delivery.
- Patients with known allergies to INH

What are the adverse effects of Isoniazid?

- Asymptomatic elevation of LFT's in 10-20% of patients receiving INH and resolves with discontinuation of the drug
- Hepatotoxicity- clinically apparent hepatitis, liver failure, and jaundice occur very rarely in those < 20 years of age; risk increases with advancing age, the post-partum period, and pre-existing liver disease.

Fatal hepatitis has occurred with continued administration of INH after onset of clinical hepatitis symptoms

- Nervous System: dizziness, headaches, fatigue, seizures, and peripheral neuropathy occur rarely
- Peripheral neuropathy: Vitamin B6 (pyridoxine) supplementation can decrease risk of peripheral neuropathy in persons who are pregnant, breast feeding, those with DM, renal failure, HIV, & alcoholism.
- Neutropenia (very rare)

What is the dosage of isoniazid (INH) for TB infection and how is it administered?

Pediatric Dosing (newborn to 11 years) INH 10 – 15 mg/kg/day	Pyridoxine Prophylaxis
3.0 – 5.0 kg = 50 mg	6.25 mg/day
5.0 – 7.5 kg = 75 mg	
7.5 – 10.0 kg = 100 mg	
10.0 – 15.0 kg = 150 mg	12.5 mg/day
15.0 – 20.0 kg = 200 mg	25 mg/day
Over 20.0 kg = 300 mg	
Adult Dosing (>11 years) INH 300 mg daily with 50 mg daily of pyridoxine	

NOTE: 6 months daily INH is an accepted alternative to 9 months of INH in adults with no other comorbidities or risk factors

Are there drug-drug interactions with INH?

- INH is a CYP3A4 inhibitor and thus increases certain substrates (e.g., Dilantin (phenytoin), carbamazepine, among others).
- INH may decrease the level of clopidogrel (Plavix) due to lack of activation of the pro-drug and consideration should be made to choose another TB regimen.
- Avoid foods high in monoamines (histamine/tyramine), such as aged cheeses, wine, fermented meats/sausages, pickled products, etc.)
<https://patienteducation.osumc.edu/Documents/DietChangesIsoniazid.pdf>



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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
 - Pregnancy and in the immediate 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 as indicated, but more frequent testing, e.g. weekly or biweekly is appropriate until the patient's pattern for hepatic chemistry testing is established
- INH should be discontinued when LFT's are ≥ 3 times normal if symptomatic of drug-induced hepatitis (e.g., anorexia and fatigue) and when LFT's ≥ 5 times normal without symptoms.

What is completion of therapy?

9 months of daily INH: complete 270 doses within 12 months.
6 months of daily INH: complete 180 doses within 9 months.

What should be done when treatment is completed?

- Patients should receive written documentation of TST or IGRA testing results, CXR results, names and dosages of medications, and duration of treatment anytime TB testing is requested.
- Providers should re-educate patients about the signs and symptoms of TB reactivation and advise them to contact a medical provider if these symptoms develop.
- Repeat CXRs are not indicated unless TB symptoms or TB disease is suspected.

Resources

Los Angeles County TB Control Program
<http://www.publichealth.lacounty.gov/tb>
213-745-0800

California Department of Public Health
Tuberculosis Control Branch (TBCB)
<http://www.cdph.ca.gov/programs/tb/Pages/default.aspx>
510-620-3000

California TB Controllers Association
<http://www.ctca.org/>
510-479-6139

Curry International Tuberculosis Center
Warmline Consultation Service
<http://www.currytbcenter.ucsf.edu/>
877-390-6682 or 510-238-5100

Centers for Disease Control and Prevention
Division of Tuberculosis Elimination
<http://www.cdc.gov/tb/>
800-232-4636

