

Isoniazid (INH) for the Treatment of TB Infection

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

How is isoniazid (INH) prescribed to treat TB infection?

INH is taken once daily for 6 to 9 months.

Is the regimen effective?

INH has historically been used as first-line treatment for TB infection. Studies indicate that a 9-month duration is ~90% effective while a 6-month regimen is ~70% 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 consisting of isoniazid + rifapentine (3HR), rifampin (4R), and isoniazid + rifampin (3HR), have much higher completion rates.

What are the advantages of this regimen?

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

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

- HIV-positive 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
- As increased hepatotoxicity has been observed during pregnancy and the early postpartum period, it is not recommended within three – six months of delivery (unless at high risk for progression to active TB disease)
- Patients with known allergies to INH

What are the adverse effects of INH?

- Asymptomatic elevation of LFT's in 10-20% of patients receiving INH which 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, during pregnancy and the early 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 INH for TB infection and how is it administered?

Pediatric Dosing 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 INH 5 mg per kg daily with 50 mg daily of pyridoxine (max 300 mg)	

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 C219 inhibitor and thus increases certain substrates (e.g., Dilantin (phenytoin), carbamazepine, among others). Closer monitoring may be considered for patients on such medications
- Avoid foods high in monoamines (histamine/tyramine), such as aged cheeses, wine, fermented meats/sausages, pickled products, etc.)
<https://www.healthwise.net/osomechart/Content/StdDocument.aspx?DOCHWID=d00101a1>

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What type of monitoring is needed for INH treatment?

- Monthly interviews and brief physical examinations to identify treatment-associated adverse events
- Baseline hepatic chemistry is recommended for patients with specific conditions:
 - HIV-positive
 - Liver disorders
 - Pregnancy and 3-6 months post-partum
 - 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
- Therapy should be discontinued or held when ALT is ≥ 3 times the upper limit of normal if symptomatic of drug-induced hepatitis (e.g., anorexia and fatigue), and when ALT is ≥ 5 times the upper limit of normal without symptoms, or total bilirubin > 3.0 . If planning to use INH + Rifampin regimen, please see guidelines "Rifampin for the Treatment of TB Infection" regarding additional considerations when using rifampin

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.
3 months of daily INH plus rifampin: complete 90 doses within 4 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 to present anytime TB testing is requested
- Providers should re-educate patients about the signs and symptoms of active TB disease and advise them to contact a medical provider if these symptoms develop
- Repeat CXRs are not indicated unless TB symptoms suggestive of active TB disease are present

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 415-502-4700

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