COMMON DRUG INTERACTIONS RELATED TO 12-DOSE (3HP) REGIMEN FOR LATENT TB INFECTION (LTBI): ISONIAZID AND RIFAPENTINE

Please note: this is ***not an exhaustive list***, and is meant to give providers an overview of drug interactions with 12-dose isoniazid and rifapentine that may be common in a primary care setting. As with any new prescription, be sure to review your patient's medication list, and consult a clinical pharmacist or medication database to review potential interactions.

General principles:

- Both rifampin and rifapentine (known as "rifamycins") are inducers of cytochrome P450 isoenzymes, thus their drug interactions are similar
- Levels of induction are higher for rifampin than rifapentine, so drug interactions tend to be more common or severe for rifampin
- Most drug interaction data comes from daily administration of rifamycins; induction is less with intermittent dosing
- Induction by rifapentine occurs within 4 days after the first dose, and is gone within 14 days after discontinuing rifapentine
- For severe isoniazid reactions not amenable to monitoring, consider use of daily rifampin x 4 months for LTBI
- For severe rifamycin reactions not amenable to monitoring, consider use of daily isoniazid x 9 months for LTBI

Table 1: Isoniazid (INH) drug interactions

Class of interaction	Drug	Interaction	Monitoring and dosage considerations
Major	Amiodarone	May result in increased amiodarone exposure	- Consult cardiologist and/or clinical pharmacist prior to prescribing
Major	Glimepiride	May result in increased glimepiride exposure and risk of hypoglycemia	- Avoid concurrent use, especially in elderly patients or those with chronic renal failure, who may have increased risk of hypoglycemia
Major	Ketoconazole	May cause decreased ketoconazole levels	- Consider need for ketoconazole and if alternate therapies are available - Avoid INH within 2 weeks of initiating ketoconazole
Major	Levodopa	As a D2 receptor agonist, INH may reduce therapeutic effects of levodopa	- Consult neurologist to discuss upward titration of anti- parkinson drugs - Monitor patient for adverse effects including agitation, flushing, palpitations, severe non-parkinsonian tremor, and elevated blood pressure
Major	Tylenol	May increase exposure to toxic acetaminophen metabolites	- Avoid or limit Tylenol use, including over-the-counter cold medications and/or combination pain medications that include Tylenol
Moderate	Phenytoin	Increase blood levels of phenytoin	- Monitor phenytoin levels while on INH - Usual therapeutic levels are 10-20 mg/L, consult clinical pharmacist for dose adjustments - Ask patients to immediately report side effects such as drowsiness, ataxia, and nystagmus
Moderate	Disulfiram	Increase blood levels of disulfiram	- Monitor patients for coordination difficulties and mood or behavioral changes - Consider dose reduction or discontinuing disulfiram
Moderate	Clopidogrel	May reduce the antiplatelet activity of clopidogrel	- Evidence on this interaction is limited - Consider indication for clopidogrel - Consider involving cardiologist and/or clinical pharmacist
Mild	Antacid	Decreased INH absorption	- Take antacids at least two hours after taking INH

Table 2: Rifapentine drug interactions

Class of interaction	Drug	Interaction	Monitoring and dosage considerations
Major	Antiretroviral therapy (ART) drugs, including protease inhibitors, darunavir, etravirine, tenofovir alafenamide (TAF)	Various mechanisms occur that can result in reduced ART efficacy and virologic failure; review comprehensive list here: https://aidsinfo.	- In persons on ART, the majority of data and clinical experience for LTBI treatment is with use of INH x 9 months - Current Department of Health and Human Services (DHHS) guidelines suggest that efavirenz or raltegravir-based regimens (in combination with either abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine) can be used with 3HP. Consider use of these regimens and 3HP with close viral load monitoring - Insufficient data characterizing interactions between other antiretrovirals and rifapentine
Major	Cancer treatment drugs	Various mechanisms	- Consult oncologist and/or clinical pharmacist - Co-administration with rifamycins generally not recommended
Major	Hepatitis C virus drugs (HCV)	Various; decrease	- Co-administration with rifamycins not recommended
Major	Oral contraceptives	Decrease blood	- Ask patient to use a back-up non-hormonal form of birth control while on rifamycins
Major	Statins (EXCEPT rosuvastatin)	Increase blood levels of statins	- Concurrent use with rifamycins not recommended - Consider use of non-interacting statin (rosuvastatin), or alternate anti-lipid agent
Moderate	Anti-arrhythmic drugs including amiodarone, and digoxin	May decrease effectiveness of anti-arrhythmic or digoxin	- Monitor serum digoxin concentrations during and after rifapentine therapy - May require increase in the anti-arrhythmic or digoxin dose - Consider possibility of antiarrhythmic toxicity after withdrawing concomitant rifapentine
Moderate	Beta-blockers (EXCEPT atenolol)	May decrease concentrati	- Monitor blood pressure and heart rate carefully - Beta-blocker dosage increase may be required
Moderate	Ciprofloxacin	May result in decreased ciprofloxacin	- Dose increases of ciprofloxacin may be required - Consider completing a course of therapy prior to prescribing rifapentine, or using alternate
Moderate	Clopidogrel	May increase antiplatelet activity of	- Evidence on this interaction is limited - Consider indication for clopidogrel - Consider involving cardiologist and/or clinical pharmacist
Moderate	Levothyroxine	May result in decreased levothyroxine	- Monitor patients for reduced levothyroxine efficacy - Levothyroxine doses may need to be increased when rifapentine is given concomitantly
Moderate	Methadone	Decrease the level or effect of methadone	- Induction is gradual with maximal effect by day 10 - May need to adjust dose until steady state (approximately within 2 weeks) - Although close monitoring is required, not a contraindication to use
Moderate	Oral hypoglycemics (including sulfonylureas, metformin)	Decrea se oral hypogly cemic effectiv	- Monitor the patient's glucose more closely during the first two to three weeks of initiating or discontinuing rifapentine - A dosage adjustment for the hypoglycemic agent may be required
Moderate	Sildenafil	Decrease blood	- Sildenafil doses may need to be increased when given concomitantly with rifapentine
Moderate	Steroids	Decrease blood	- Steroid doses may need to be increased while on rifapentine
Moderate	Warfarin	Decrease blood levels of	- Induction is gradual with maximal effect by day 10 - Not contra-indicated, but a significant interaction that requires close monitoring of international normalized ratio