

Isoniazid and Rifapentine for Treatment of Latent TB Infection – Guidelines for Use

Indications

The isoniazid-rifapentine regimen is Indicated for treatment of latent TB infection in persons two years of age or older and is specifically recommended for persons anticipated to be difficult to reach or treat and those that would benefit from a shorter course of treatment.

Contraindications to Rifapentine Use

- Known hypersensitivity to any rifamycin.
- Rifapentine is not recommended for:
 - Those presumed to be infected with a rifampin or isoniazid resistant strain;
 - Children less than two years of age as data on the safety and pharmacokinetics of rifapentine for this age group is not available; and Women that are pregnant or expecting to become pregnant within the 12 week period of treatment as safety in pregnancy is not known.

Cautions and Drug Interactions

- Use with caution when interacting medications are administered concomitantly (e.g., methadone and warfarin).
- Women on hormonal birth control shall be advised to add, or switch to, a barrier method of birth control to prevent pregnancy.
- Women that are breastfeeding should either discontinue breastfeeding or be prescribed another regimen for treatment of latent TB infection. It is not known if rifapentine is present in breast milk and there may be a risk of adverse reactions in the breastfeeding infant.

Requirements Prior to Treatment Initiation

1. Active TB must be ruled out within one month of the anticipated treatment start date.
2. Baseline blood work must be completed and reviewed by the TB physician. See table 1.
3. Directly observed therapy must be arranged; self-administered therapy is not permissible.
4. Education regarding the medications and treatment plan must be provided for the client and/or family.

Treatment Completion

Treatment completion is defined as 12 doses taken within 16 weeks of treatment initiation.

Dosage for Isoniazid-Rifapentine Regimen

Isoniazid	
Adults and children aged 12 years and older: 15 mg/kg rounded up to the nearest 50 or 100 mg	
Children 2 to 11 years of age AND weighing at least 10 kg: 25 mg/kg	
Maximum dose all ages – 900 mg	
Rifapentine	
10 – 14 kg	300 mg
14.1 – 25 kg	450 mg
25.1 – 32 kg	600 mg
32.1 – 49.9 kg	750 mg
50 kg or more	900 mg (maximum)
Pyridoxine	
Prophylaxis for isoniazid-associated neuropathy should be considered especially for persons who are malnourished or predisposed to peripheral neuropathy due to other conditions.	
Adults and children aged 12 years and older: 50 mg	
Children 2 to 11 years of age: 1 mg/kg	

Source: MMWR/December 9, 2011/Vol. 60/No. 48; Lexicomp Online – Rifapentine monograph, Isoniazid monograph, Pyridoxine monograph

Administration

1. Isoniazid-rifapentine will be given once weekly, on Mondays, by DOT.

Note: The day of the week for once weekly DOT may be changed on an ongoing basis if necessary due to workload or client preference provided it is approved by the TBPC SK Nurse Clinician.

2. Each dose must be separated by at least 72 hours. If the dose is missed on Monday it may be given on Tuesday, Wednesday or Thursday.

Note: For practical purposes, a missed dose should not be given on Friday as the dose on Monday will need to be given at the same time, or later, to ensure at least 72 hours separates the two doses.

3. TB physician review must occur if two consecutive doses are missed. In such cases, consideration should be given to discontinuing the isoniazid-rifapentine regimen and changing the treatment regimen to rifampin alone.
4. The medications should be given with food.
5. Prior to the first client's treatment initiation within a given community or clinical setting, education for local health-care providers will be provided by TBPC SK or designated partners.

Clinic Follow-up:

1. Monthly TB clinic follow up will be scheduled at the request of the TB physician.
2. The TB Prevention and Control Saskatchewan (TBPC SK) Nurse Clinician will complete a nursing assessment each month when clients are receiving DOT from an unregulated care provider.

Arrangements will be made for the local or point-of-care nurse to complete the assessment when the client does not have phone access.

Monthly nursing assessment will include, but is not limited to:

- verification of adverse effects;
- medication review; and
- questioning regarding potential pregnancy for women of childbearing age.

Note: Monthly nursing assessment is not required if the client will be assessed in the TB clinic. It is also not required if a Registered Nurse, Licensed Practical Nurse, or Registered Psychiatric Nurse is delivering DOT as nursing assessment is ongoing and occurs with each dose.

Monitoring

Table 1: Treatment Monitoring and Follow-up Schedule for Isoniazid-Rifapentine		
Activity	Baseline	Ongoing
HIV testing ¹	Yes, if previously negative	Not required
Complete blood count	If pre-existing conditions ²	As ordered by TB physician
Electrolytes 6 ³	If pre-existing conditions ²	As ordered by TB physician
Liver function tests ⁴	If pre-existing conditions ²	Every 2-4 weeks if baseline testing abnormal or pre-existing liver disease. Every 4 weeks for all other pre-existing conditions.
Sputum	Yes, if symptomatic or clinically indicated	Yes, if symptomatic or clinically indicated
Chest x-ray	Prior to treatment initiation to rule out active TB	As ordered by TB physician
TB clinic	Yes, if feasible	Monthly – see additional information under Clinic Follow-up
Medication audits	Not applicable	Monthly and more often as indicated.
Height and weight	Yes	As ordered by TB physician

¹ HIV testing will be offered to children 13 years of age and older. Testing will be offered to children less than 13 years of age at the discretion of the TB physician.

² Pre-existing conditions include liver disease, IV drug use, HIV infection, excess alcohol consumption, less than 3 months post-partum, or receiving hepatotoxic drugs.

³ Electrolytes 6 include sodium, potassium, chloride, bicarbonate, creatinine, and urea. Calcium, magnesium and phosphate will be completed as ordered by the TB physician.

⁴ Unless otherwise indicated by the TB physician, liver function tests will include AST, ALT, ALP, GGT, and bilirubin (direct and indirect).

Adverse Effects (based on combination therapy):

1. The Adverse Effects Checklist must be completed before each dose, including the first dose (see Figure 1). The dose shall be withheld if the client is experiencing any of the symptoms listed. The TBPC SK nurse clinician must be notified immediately if the client experiences any symptoms.
2. The completed Adverse Effects Checklist label shall be affixed to the reverse side of the TBPC SK Medication Record and both sides of the record faxed to the TBPC SK nurse clinician following each dose.
3. Consideration should be given to discontinuing the isoniazid-rifapentine regimen and changing the treatment regimen to isoniazid alone when clients are experiencing adverse effects.
4. Adverse reactions must be reported to TBPC SK in addition to being documented and reported in accordance with agency policy. TBPC SK will report serious adverse drug reactions to Health Canada using the Canada Vigilance Side Effect Reporting [form](#) or by completing the online report at <https://hpr-rps.hres.ca/static/content/form-formule.php?lang=en> .

Note: A serious adverse drug reaction means "...a noxious and unintended response to a drug that occurs at any dose and that requires in-patient hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death. This definition implies that the causal relationship between the drug and the occurrence of the adverse reaction is suspected." (Questions and Answers: Access to Drugs in Exceptional Circumstances, 2017, p. 13)

Figure 1: Adverse Effects Checklist

ADVERSE EFFECTS CHECKLIST					
Name: _____					
TB File #: _____		Date: _____		Dose #: _____	
Signature & position: _____					
DO NOT GIVE DOSE and CALL TBPC RN if YES to any symptom					
Symptom	Yes	No	Symptom	Yes	No
Hives			Weakness or fatigue		
Dizziness			Vomiting		
Wheezing			Abdominal pain		
Swelling eyes, lips, tongue, throat, skin			Aches		
Itchy eyes			Yellow eyes		
Shortness of breath			Itching		
Flushing, chills, sweats			Bruising, easy bleeding		
Fever			Rash		
Peel and stick to reverse side of TB Medication Record					
TB Prevention and Control Saskatchewan 2018-11-22					

References:

Jereb, JA, Goldberg SV, Powell, K, et al. [Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection](#). MMWR Morb Mortal Wkly Rep 2011; 60: 1650-1653.

Borisov AS, Bamrah Morris S, Njie GJ, et al. Update of Recommendations for Use of Once-Weekly isoniazid-Rifapentine Regimen to Treat Latent *Mycobacterium tuberculosis* infection. MMWR Morb Mortal Wkly Rep 2018; 67:723-726. DOI: <http://dx.doi.org/10.15585/mmwr.mm6725a5>.

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