NTCA PROVIDER GUIDANCE

A 4-Month Regimen to Treat Pulmonary Tuberculosis: Isoniazid, Rifapentine, Moxifloxacin, and Pyrazinamide (HPMZ)

What is the 4-month HPMZ Regimen for treatment of drug susceptible TB?

The HPMZ regimen consists of an **8-week intensive phase** of isoniazid (H), rifapentine (P), moxifloxacin (M), and pyrazinamide (Z) given daily, followed by a **9-week continuation phase** of isoniazid, rifapentine, and moxifloxacin given daily. The total duration of therapy is 17-weeks.

What is the medication dosage of the HPMZ regimen?

Medication	Body weight	Dose/day
Isoniazid (INH, H)	> 40 kg (88 pounds)	300 mg
Rifapentine (RPT, P)	> 40 kg (88 pounds)	1200 mg
Moxifloxacin (MOX, M)	> 40 kg (88 pounds)	400 mg
Pyrazinamide (PZA, Z)	40–<55 kg (88–121 pounds)	1000 mg
	>55–75 kg (121–165 pounds)	1500 mg
	> 75 kg (> 165 pounds)	2000 mg

The entire regimen should be administered once daily with food 7 days per week.

What are the advantages and disadvantages of the HPMZ Regimen?

Potential pros of the 4-month regimen

- A shorter duration of treatment for culture-positive pulmonary TB.
- Facilitates treatment completion in patients with barriers
  - planned geographic relocation, incarceration, or
  - residents in congregate or institutionalized settings
- Avoids potential for ocular toxicity with ethambutol (EMB)
- May reduce time to culture conversion

Potential cons of the 4-month regimen

- Higher pill burden
- Required to be taken with food to optimize drug absorption.
- Avoid drug-drug interactions with comedications (e.g., antacids)
- Potentially higher program cost for HPMZ regimen
- Limited long-term outcome data (12 months post-randomization)
- Potential side effects of fluoroquinolone (e.g., QT prolongation, tendonitis, effects on gut microbiota)
- Lack of data for treating extrapulmonary TB, including CNS disease and osteomyelitis

	Standard Regimen (HRZE) >75Kg	Short course regimen (HPMZ) >75Kg
Intensive Phase	8 weeks  Isoniazid Rifampin Pyrazinamide Ethambutol Vitamin B6	8 weeks  Isoniazid Rifapentine Moxifloxacin Pyrazinamide Vitamin B6
Continuation Phase	16-28 weeks  Isoniazid Rifampin Vitamin B6	9 weeks  Isoniazid Rifapentine Moxifloxacin Vitamin B6

Photos courtesy of George Lee, RN

Treatment interruption:

- The 56 doses of initiation phase should be administered completely within 70 days.
- The 63 doses of the continuation phase should be administered within 84 days.
- If these targets are not met, the patient should be considered to have interrupted therapy and should be managed with clinical judgment and in consultation as described in TB treatment guidelines.

Are there drug-drug interactions?

There are common interactions for isoniazid, rifapentine, and moxifloxacin:

- Isoniazid increases blood levels of phenytoin and disulfiram
- Rifapentine, similar to rifampin, decreases blood levels of oral or implanted hormonal contraceptives, warfarin, sulfonylureas, methadone, suboxone, some anti-hypertensives and steroids.
- Some cardiac medications and certain antiretroviral drugs may have serious drug-drug interactions.
- Moxifloxacin interacts with other medications that are QTc prolonging. Please see additional information on use of moxifloxacin under Programmatic Consideration (Page 2).
- **Please check drug-drug interactions**

Possible adverse events (AEs) with HPMZ

Mild to moderate:

Continue to monitor, discontinue if needed

- Joint pain
- Tendonitis
- LFTs ≥ 3-5X ULN
- Rash
- Fever
- Pruritis
- Nausea
- Vomiting

Moderate to Severe:

Recommend discontinuing treatment

- Hypersensitivity
- Hypotension, mild to profound syncope/fainting
- Dizziness
- Life threatening syndromes (fever, chills HA, dizziness and musculoskeletal pain)
- Thrombocytopenia
- Shortness of breath, wheezing, acute bronchospasm
- Urticarial petechiae, purpura
- Conjunctivitis
- Angioedema and shock
- Chest pain/angina, palpitations, or cardiac arrhythmias
- Elevated liver function tests (LFTs) ≥ 5X ULN

Patient checklist before starting HPMZ

- ✔ Age ≥ 12 years
- ✔ Weight > 40 kg
- ✔ If HIV-positive, CD4>100 cells/mm^3, please see NTCA FAQ for additional HIV treatment recommendations.
- ✔ Negative pregnancy test if of childbearing age
- ✔ Not breastfeeding
- ✔ Baseline laboratory values: serum creatinine < 2.0, potassium ≥ 3.5 meq/L, Hgb ≥ 7.0 g/dL, platelets ≥ 100,000/mm^3, LFTs ≤ 2X upper limit of normal
- ✔ No suspected or documented extrapulmonary TB
- ✔ No history of taking TB drugs within past 6 months
- ✔ Medication review with no drug–drug interactions with HPMZ
- ✔ Rapid molecular detection of drug resistance from initial specimen should be ordered if available
- ✔ Patient can be started on the HPMZ regimen while awaiting drug susceptibility test (DST) results, including for fluoroquinolones

Programmatic Considerations for HPMZ

Case management:

- Ensure drug supply available for full 17-week course
- Discuss pill burden and need for once-daily dosing
- Medications taken 7 days a week and DOT/eDOT at least 5 days a week
- Monthly clinical visits
- Sputum, laboratory, and EKG monitoring when indicated
- Verify reimbursement for HPMZ by program or third party

Moxifloxacin

- Educate about food and drug interactions: Avoid taking dairy products, sucralfate, antacids, multivitamins, iron, aluminum, magnesium, or calcium within 4 hrs. before or 8 hrs. after HPMZ
- Access EKG for patients with cardiac risks per practice standards for long term moxifloxacin administration.
- Review cardiac history: This regimen is contraindicated in patients with active ischemia and/or history of arrhythmias.
- CDC does not recommend use with other medications that prolong QTc; however, some experts may choose to prescribe this regimen in patients with h/o prolonged QTc or patients on other QT-prolonging drugs with careful and appropriate EKG monitoring.

Rifapentine

- Discuss FDA alert regarding nitrosamine with patient

Baseline and follow-up monitoring and evaluation for patients on HPMZ regimen

(**X** = recommended; **O** = optional)

Evaluation Types

			Intensive Phase (Total 56 doses)								Continuation Phase (Total 63 doses)								
		Baseline	Week **1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
Clinical assessment and evaluation	Symptoms, medication, drug–drug interaction	X				X				X				X					X
	Weight	X				X				X				X					X
	EKG if indicated	O				O				O				O					O
Laboratory testing	CBC, Platelet, LFT, Creatinine, Potassium, Calcium, Magnesium	X				O				O				O					O
	HIV (if positive CD4 count and HIV RNA)	X																	
	Hepatitis B and C Diabetes screen	O																	
	Pregnancy test	X																	
Microbiology (Sputum)	AFB smear and culture	X	O	O	O	X				X				O					O
	Rapid molecular test	X																	
	Phenotypic drug susceptibility test	X								O									
Imaging	Chest radiograph	X								O									O
Administered medication **DOT/eDOT with food ≥ 5 days/ week**	Isoniazid (INH, H)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Rifapentine (RPT, P)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Moxifloxacin (MOX, M)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Pyrazinamide (PZA, Z)		X	X	X	X	X	X	X	X									
	Vitamin B6		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Consultation with TB clinical experts at either local or state level, or TB Center of Excellence (COE) recommended:

- For treatment of lymph node or pleural disease.
  - Avoid using this regimen for sites such as as with CNS or bone disease
- For concerns regarding slow or incomplete clinical response or treatment failure
- For interruption in therapy or changes in drug regimen

Please refer to the full NTCA FAQ for detailed discussion of the HPMZ regimen:
https://www.tbcontrollers.org/docs/resources/4-Month-HPMZ-TB-Regimen_NTCA-FAQ.pdf