NATIONAL TPT WEBINAR

Strengthening TB Prevention

Evidence, eligibility and correct use of 3HP

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Clinical management of patients on 3HP · August 2026

POLL 1

Thandi, 34. Living with HIV, on TLD for two years, VL <50 c/mL. Weight 58 kg. No TB symptoms. Which TPT would you prescribe?

A 12H — isoniazid daily for 12 months

B 3HP — weekly rifapentine + isoniazid

C 3RH — daily rifampicin + isoniazid

D She isn't eligible for TPT

SESSION OUTLINE

What we'll cover...

1. **Evidence**
   What 3HP is and why it works
2. **Eligibility**
   Who qualifies — and which guideline governs
3. **Pregnancy**
   A position that has changed four times
4. **Prescribing**
   Dose, food, pyridoxine, monitoring
5. **Adverse events**
   Recognise, grade, act
6. **Interruption**
   Missed doses and pharmacovigilance

THE REGIMEN

What 3HP actually is

- **12 once-weekly doses**

  Rifapentine + isoniazid, taken over 12 weeks

- **Rifapentine is a rifamycin**

  Same interaction class and broadly the same side-effect profile as rifampicin

- **Treats infection, not disease**

  Active TB must be excluded before every initiation

FOR PHARMACISTS

Rifapentine 150 mg or 300mg or co-formulated with INH 300mg/300mg

Do not confuse rifapentine with rifampicin or rifabutin at the dispensing point.

This is a documented dispensing error, not a theoretical one.

12 doses. 12 weeks. 16-week completion window. That window is the built-in leeway for missed doses.

WHY A THREE-MONTH REGIMEN

The evidence, briefly

3HP is neither inferior nor superior to isoniazid on efficacy or safety. The argument for it is completion and tolerability.

19.7%

vs 34.1%

Modelled discontinuation: 3HP vs 12H

Lower

than daily INH

Rate of hepatotoxicity

NNT 33

NNT 57 for mortality

To avert one TB case in non-pregnant PLHIV

Underlying TPT benefit in PLHIV

≈33% reduction in TB disease overall (RR 0.67, 95% CI 0.51–0.87) · ≈64% where infection is proven (RR 0.36, 0.22–0.61)
South African cohort, mostly on ART: 37% reduction (HR 0.63, 0.41–0.94), protective even in TST/IGRA-negative patients

Sources: SA budget impact analysis, June 2022; Akolo Cochrane review; Rangaka 2014; NEMLC review 2018.

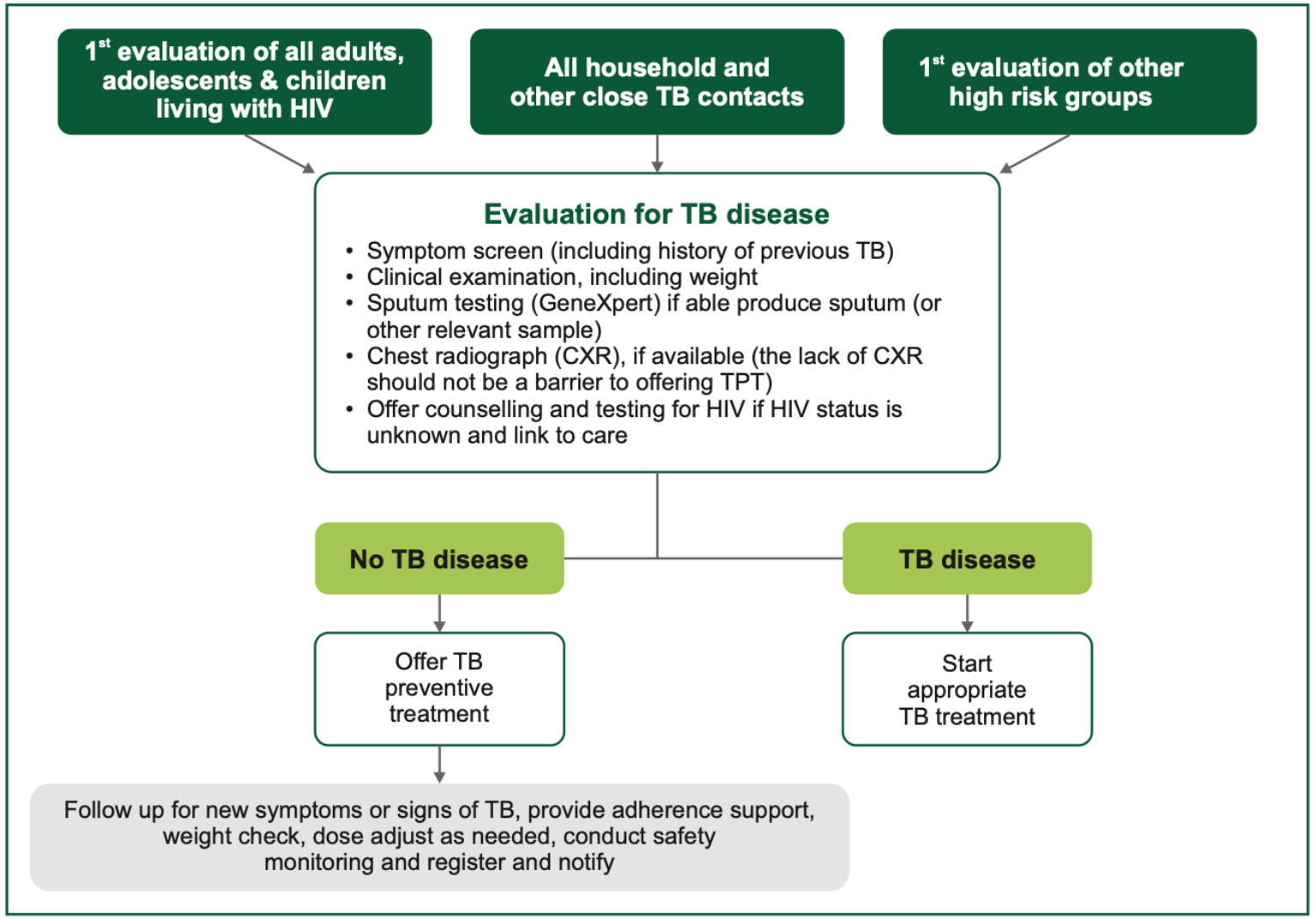
GUIDELINE ALIGNMENT

Which document governs what

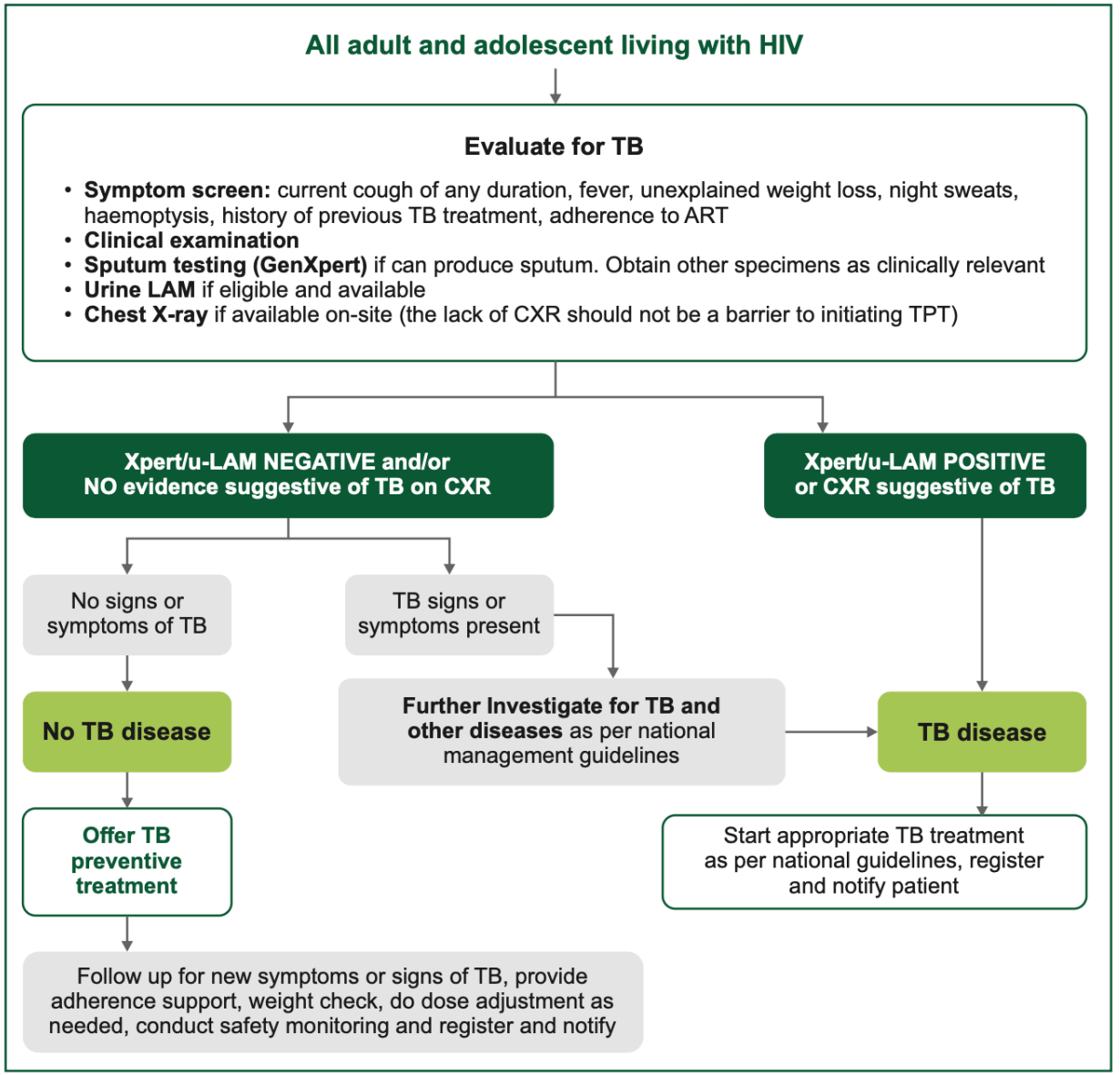
Photograph this one.

Source	Use it for
National Consolidated Guidelines **May 2026**	Anything involving people living with HIV — this is current
PHC STG / EML, 8th edition **March 2026**	Primary-care prescribing detail
National Guidelines on the Treatment of TB Infection **February 2023**	HIV-negative contacts and non-HIV at-risk groups — not covered by either 2026 document
Interim Clinical Guidance on the Use of 3HP **2020, unsigned**	Clinical care process — but see the update slide later in this session

General algorithm for provision of TB preventive treatment using the test and treat approach



Algorithm for provision of TB preventive treatment for adults and adolescents living with HIV



ELIGIBILITY

Who gets 3HP

Adults, adolescents and children ≥ 25 kg who are:

✓ **Virally suppressed on DTG**

VL < 50 c/mL in the last six months

✓ **ARV naïve and not on a DTG-containing regimen**

Provided no protease inhibitor is in use

✓ **HIV-negative and in an eligible group**

Close contacts, silicosis, dialysis, anti-TNF therapy, diabetes, transplant candidates, previously treated on re-exposure

The 25 kg threshold is a weight criterion, not an age criterion. This changed in 2023 and is still applied inconsistently.

EXCLUSIONS

Who does not get 3HP

Newly initiating on DTG

Use 12H. Not negotiable in current guidance.

Protease inhibitor–based ART

Use 12H.

Children < 25 kg

6H if living with HIV on DTG. 3RH if HIV-negative. 6H for HIV-exposed infants on nevirapine — rifampicin drops nevirapine below efficacy.

Pregnancy

Not 3HP. See the pregnancy section.

Also excluded, whatever the ART regimen

Active liver disease · Alcohol abuse · Painful peripheral neuropathy · Previous MDR- or XDR-TB · Known isoniazid hypersensitivity

PRE-INITIATION

Before you prescribe

1	**Exclude active TB**	Clinically and by testing. A TST or IGRA is not required.
2	**Don't wait for the NAAT**	If the patient is asymptomatic, start. Results can follow.
3	**Well children**	No Need for sputum nor chest X-ray to start.
4	**Same day is fine**	ART and TPT can be initiated on the same day.
5	**Baseline LFTs**	Not routine in South Africa. Consider where risk concentrates: known liver disease, heavy alcohol use, postpartum ≤ 3 months.

POLL 2

Thandi is on the two-monthly injectable contraceptive. Can she have 3HP?

A Yes — injectables are unaffected

B Yes, if she also uses condoms

C No

D I'm not sure

THIS HAS CHANGED

Contraception: what changed, and when

FEBRUARY 2023

Rifapentine lowers oral and implant levels — use a barrier method, offer an injectable.

superseded

MARCH 2026 — STG

Do not use rifapentine-containing TPT in women on hormonal contraceptives.

the change enters here

MAY 2026 — NCG

Do not use rifapentine-containing TPT in women on oral or injectable contraceptives.

current

Both 2026 documents exclude the injectable.

What to do on Monday

Do not use 3HP in women on any hormonal method.
Offer a copper IUCD or barrier method, or use 12H. This satisfies both 2026 documents and errs safe.

What to do

Follow May 2026. Offer a non-hormonal method — copper IUD — or use 12H.

Pharmacists: rifapentine also lowers warfarin, sulfonylureas, methadone, corticosteroids and some cardiac drugs. Isoniazid raises phenytoin and disulfiram. Review every chronic prescription at initiation.

POLL 3

Newly diagnosed with HIV at her first antenatal visit. CD4 156. No TB symptoms. What TPT?

A 3HP

B 12 months of isoniazid

C Defer to post-partum

D 3RH

TPT IN PREGNANCY

Pregnancy and TPT

When	Position	
Feb 2023	12H for all HIV-positive pregnant women, at any CD4 count	*superseded*
Mar 2024	Defer TPT in all pregnant women — decided on feasibility grounds	*superseded*
Nov 2025	ERC and NEMLC reinstate stratification at CD4 200, nested in the AHD package	*evidence base*
May 2026	**CD4 ≤ 200 or WHO stage 3/4 → 12 months isoniazid.** **Above 200 → defer to post-partum. TB screening at every antenatal visit.**	**CURRENT**

Note: **this refers to isoniazid, not 3HP. 3HP remains not recommended in pregnancy.**

THE REASONING

Why the threshold sits at 200

Below CD4 200

The benefit of preventing TB disease outweighs the harm. These women are already eligible for the advanced HIV disease package, which contains IPT — so this nests inside an existing pathway rather than standing alone.

Above CD4 200

Harm outweighs benefit: increased miscarriage after first-trimester exposure, and increased low birth weight plus underweight-for-age after second-trimester exposure. CD4 350 was considered but judged programmatically unworkable.

Dosing

Body weight (kg)	Rifapentine	Isoniazid	Duration
	150mg tablets (weekly)	300mg tablets (weekly)	
25-29.9	4	2	12 weeks (3 months)
30 – 49.9	6	3	12 weeks (3 months)
>50	6	3	12 weeks (3 months)

Note: If 3HP is not available, 3RH should be used in adults, adolescents and children ≥25kg without HIV. Alternatively, 6H can be used.

COUNSELLING AT INITIATION

How the patient takes it

1 The whole weekly dose at once	Same day every week for 12 weeks. Choose the day with the patient and write it down.
2 With food, or directly after a meal	Rifapentine absorbs better with food.
3 Isoniazid regimens are the opposite	6H, 12H and 3RH go on an empty stomach — isoniazid loses up to 50% of peak concentration with a fatty meal.
4 Red-orange urine, sweat and tears	Normal and harmless. Warn about staining of soft contact lenses and light clothing. Unwarned patients stop treatment over this.
5 Pyridoxine 25 mg daily	Daily, not weekly, for the full duration.

MONITORING

The monthly visit: five checks

1. **Screen for active TB**
2. **Screen for pregnancy**
3. **Screen for adverse events**
4. **Assess adherence**
5. **Check for new interacting drugs**

New in May 2026 — and it answers the commonest objection to 3HP

In repeat prescription collection models, the full three-month 3HP supply can be scripted with no additional clinician review visit. This removes the extra-visit caveat that sat in Annexure C of the 2023 guidelines.

POLL 4

Week 3. Four hours after her dose, a patient develops fever, headache, muscle aches and dizziness. What do you do?

A Continue — treat symptomatically

B Withhold this dose, manage symptoms, re-challenge next week

C Stop 3HP permanently

D Refer immediately

INTERIM CLINICAL GUIDANCE, TABLE 4

Managing side effects

Presentation	Action	Continue 3HP?
GI distress	Rule out other causes. Liver function tests to exclude drug-induced hepatic dysfunction.	**Yes — based on severity**
Mild rash	Treat symptomatically if no other cause is found. Patient stops and returns to clinic if it worsens.	**Yes**
Flu-like syndrome	Do not take the next dose. Ancillary treatment as needed — bronchodilators, steroids. Monitor.	**Withhold, then re-challenge at the next dose if symptoms resolve**
Severe hypersensitivity	Antihistamines, steroids, urgent supportive care. Refer for further assessment.	**No — discontinue**

Note

Hypersensitivity typically appears after the first three to four doses and begins roughly four hours after ingestion. That timing is what separates it from an incidental viral illness.

A FOUR-STEP SEQUENCE

Assessing any adverse event

Advise the patient to take no further doses until the assessment is done.

1. **Screen for active TB**
   TB disease can present as an adverse event
2. **Take a past history**
   Prior reactions, comorbidity, concurrent drugs
3. **History of the event**
   Type, onset, duration, severity
4. **Relevant examination**
   Directed by the presenting complaint

Severe reactions: seek urgent supportive care

Mild to moderate: reassurance, symptomatic relief, further assessment

Refer urgently and stop treatment immediately for: new-onset vomiting, right upper quadrant pain, or jaundice.

Adverse Events and Management

Adverse Event	Drug(s) Responsible	Signs/ Symptoms	Management
Peripheral Neuropathy	Isoniazid(H)	Tingling or burning sensation of the fingers and/or toes that usually occurs in a glove and stocking distribution	Vitamin B6 (pyridoxine) must be increased from 25 mg to 100 mg daily until the symptoms disappear. If the peripheral neuropathy is severe or worsens, then H should be discontinued immediately.
Hepatotoxicity	Isoniazid(H) Rifapentine (P)	Symptoms: nausea, vomiting, abdominal tenderness, discomfort near the ribs on the right upper abdomen, jaundice (yellowing of skin and whites of the eyes) Signs: Hepatic enlargement, increased LFTs	Stop Isoniazid or Rifapentine immediately, Refer the patient to the hospital/ medical officer immediately for further evaluation.
Gastrointestinal Uncommon at recommended daily doses	Isoniazid(H) Rifampicin (R) Rifapentine (P)	Symptoms: nausea, vomiting, diarrhoea	Rule out other causes Conduct liver function tests to rule out drug-induced hepatic dysfunction Continue treatment based on severity of symptoms Treat symptomatically (if no other cause is found)
Flushing reaction	Isoniazid (H)	Symptoms: Flushing and/or itching of the skin with or without a rash, hot flushes, palpitations, headache Signs: increased blood pressure	Reassure patients and inform about avoiding tyramine and histamine-containing foods (e.g. tuna, cheese red wine) while receiving Isoniazid Flushing is usually mild and resolves without therapy If flushing is bothersome to the patient, an antihistamine may be administered to treat the reaction
Mild itching Rash	Isoniazid (H) Rifapentine (P)	Mild rash and itching	Treat with antihistamine Prednisone may be added at 40mg/day and tapered gradually as the rash clears A topical cream may be added.
Hypersensitivity uncommon Usually occurs 3 - 7 weeks after initiation of treatment	Isoniazid (H)	Symptoms: hives (raised, itchy rash) fever (may occur)	Discontinue treatment until the reaction resolves
Hypersensitivity reaction occurs after the first 3–4 doses and begins approximately 4 hours after ingestion of medication	Rifapentine (P)	Symptoms: flu-like symptoms, fever, headache, dizziness, shortness of breath, wheezing, nausea, muscle and bone pain, rash, itching, red eyes, hypotension or shock	If mild reaction e.g. rash, dizziness, fever: continue treatment and manage the AEs If severe reaction e.g. thrombocytopenia, hypotension, discontinue treatment and refer to hospital

THE DOCUMENT BEHIND THE CURRENT ONLINE TRAINING

Where the interim guidance needs updating

Interim Clinical Guidance, 2020	Current Guidelines
PLHIV aged 15 and over only	**Weight-based, ≥ 25 kg — and HIV-negative groups included**
Pyridoxine weekly	**Pyridoxine daily**
Excludes newly diagnosed PLHIV starting TLD	**Defined by viral suppression, not by timing of diagnosis**
Injectable contraception acceptable	**Injectables now excluded**
Numeric alcohol thresholds	**Varies by document — use structured assessment**

Everything else still stands — the side-effect table, the interruption rules and the pharmacovigilance algorithm remain the best clinical content we have.

TREATMENT INTERRUPTION, PART 1

Missed doses

Missed on the day	Take it as soon as remembered, same day.
Within 3 days	Take it, then continue on the usual day.
More than 3 days	Either skip it and resume the usual day, adding a week at the end — or start a new weekly schedule on the day remembered. Both are acceptable. Choose one with the patient and write it down.

12 doses within 16 weeks = completion.

The 16-week window is the built-in leeway. Eleven doses in 16 weeks counts as sufficient though not ideal — for rare and insurmountable circumstances only.

TREATMENT INTERRUPTION, PART 2

Longer interruptions

CONTINUE

Under 1 month

Ask why. Address concerns. Counsel on adherence. Screen for TB — investigate if symptomatic. If asymptomatic, continue and complete the remaining doses.

RESTART

1 month or more, first interruption

Reassess eligibility. Intensive counselling. Restart the regimen. Refer for social support where indicated.

STOP

Second interruption, any duration, despite counselling

Do not consider for retreatment.

For short regimens the interruption threshold is four consecutive weeks — not the three months used for 6H and 12H.

Events during the course

Event	Action
Active TB or TB symptoms	Discontinue 3HP. Investigate; treat per national guidelines if positive.
New or changed chronic medication	Document type, interactions and dose. Continue only if safe to do so.
Malaria	Continue if not severe; treat per national guidelines. Withhold if severe.
Other febrile illness	Rule out active TB. Withhold, investigate, and resume if TB negative.
Pregnancy	Discontinue 3HP. Then, per May 2026: CD4 ≤ 200 or WHO stage 3/4 → 12 months isoniazid. Above 200 → defer to post-partum.

INTERIM CLINICAL GUIDANCE, FIGURE 3

Drug–drug interactions: the mechanism

Most interactions run through cytochrome P450. The two drugs in 3HP act on it in opposite directions.

ISONIAZID · INHIBITOR

Raises the levels of

- Anticonvulsants
- Anticoagulants
- Efavirenz
- Some SSRIs
- Antifungals
- Antipsychotics
- Antimalarials — halofantrine

RIFAPENTINE · INDUCER

Lowers the levels of

- **Hormonal contraceptives**
- **Protease inhibitors and nevirapine**
- Anticoagulants — warfarin
- Sulfonylureas
- Corticosteroids
- Cardiac glycosides — digoxin
- Antifungals, antipsychotics, antimalarials

The shortcut: rifapentine is a rifamycin. If a medicine interacts with rifampicin, assume it interacts with rifapentine. Review every chronic prescription at initiation and at each monthly visit.

INTERIM CLINICAL GUIDANCE, FIGURE 4 AND TABLE 7

Drug–drug interactions: antiretrovirals

CAN BE CO-ADMINISTERED

Efavirenz
No dose adjustment required

Raltegravir

Dolutegravir — only if virally suppressed
No dose adjustment in stable PLHIV on ART who are suppressed (DOLPHIN)

DO NOT GIVE 3HP

Protease inhibitors
e.g. lopinavir/ritonavir

Nevirapine, and most NNRTIs

ART-naïve patients starting dolutegravir
In every case: offer isoniazid monotherapy instead

A patient on a protease inhibitor does not need to go without TPT.
Either offer isoniazid monotherapy, or — where the ART regimen can be changed on other grounds — an efavirenz, dolutegravir or raltegravir-based regimen allows 3HP.

Contraception

Both 2026 documents now exclude rifapentine-containing TPT in women on hormonal contraception altogether. Use a copper IUCD or barrier method, or use 12H.

PHARMACOVIGILANCE

Reporting adverse events

Which form

ADR reporting form at Annexure 15 of the May 2026 Consolidated Guidelines, and to SAHPRA.

What to report

Record and report adverse events wherever possible. Serious events are rare, which is precisely why each one carries signal value for the programme.

The threshold should be lower, not higher

We give TPT to people who are not sick. Because the person in front of you has no disease to be cured of, the acceptable threshold for harm is far lower than in treatment — and so the threshold for reporting should be too. Pharmacovigilance is what protects the programme's licence to scale.

CLINICAL CASE

Meet Ms N

Ms N, 29 years old, at a PHC clinic. Living with HIV for three years, on TLD. Viral load < 50 c/mL six weeks ago. Weight 58 kg.

Her brother was diagnosed with sputum-positive pulmonary TB last month and lives in the same house.

No cough, no fever, no night sweats, no weight loss.

Is she TPT eligible? Which regimen, what dose, and what do you need before you prescribe?

CLINICAL CASE · DECISION 2

Ms N, continued

As you write the script, she mentions that she gets the two-monthly injectable contraceptive at family planning.

Does anything change?

CLINICAL CASE · DECISION 3

Ms N, continued

She opts for a copper IUD and starts 3HP.

At dose 3 she phones the clinic: four hours after taking her tablets she has fever, headache, myalgia and dizziness. She feels better by the evening.

What is this, and what do you do?

CLINICAL CASE · DECISION 4

Ms N, continued

She tolerates the re-challenge. She then misses dose 7 and returns 10 days later.

At week 9, she tells you she is pregnant.

How do you manage the missed dose — and what happens now?

POLL 5

Back to Thandi. On TLD two years, VL <50 c/mL, 58 kg, no TB symptoms. Which TPT would you prescribe?

- **A** 12H — isoniazid daily for 12 months
- **B** 3HP — weekly rifapentine + isoniazid
- **C** 3RH — daily rifampicin + isoniazid
- **D** She isn't eligible for TPT

SUMMARY

Seven things to take back to your facility

1. The May 2026 Consolidated Guidelines are current for people living with HIV
2. 3HP only if virally suppressed on DTG — never at DTG initiation, never with protease inhibitors
3. **Not with oral or injectable contraception. This has changed.**
4. 3HP with food. Isoniazid regimens on an empty stomach.
5. Pyridoxine daily, full three-month script, monthly review
6. Flu-like reaction after doses 3–4: withhold and re-challenge, don't abandon
7. Pregnancy: CD4 ≤ 200 or WHO stage 3/4 → 12H; otherwise defer to post-partum

Thank you

Uptake, supply and implementation — over to Dr Mvusi.

Remaining clinical questions are welcome in the panel discussion .