



health

Department:  
Health  
REPUBLIC OF SOUTH AFRICA



Reference: AMD/07February25

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**NOTICE: SUPPLY CONSTRAINTS WITH RIFAMPICIN-BASED COMBINATIONS (RIFAMPICIN/ISONIAZID (150/75MG AND 300/150MG FORMULATIONS)) FOR TUBERCULOSIS (TB) TREATMENT - INTERIM THERAPEUTIC ALTERNATIVES RECOMMENDED BY THE AFFORDABLE MEDICINES DIRECTORATE**

***Note: The guidance presented below takes into consideration the latest supply chain information on essential medicines for TB. We therefore urge healthcare professionals to utilise the guidance presented below, to ensure adequate availability of medicines to manage TB during this period of constrained supply.***

The Primary Healthcare, Adult Hospital Level and Paediatric Hospital Level Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) currently recommends the use of rifampicin/isoniazid (RH) 150/75mg and 300/150mg for the continuation phase of TB disease and TB Preventive Therapy. There is currently insufficient supply of RH to meet the national demand.

To ensure continuity of care, while the supply of RH remains unstable, rifapentine in combination with isoniazid may be used in the continuation phase, as an alternative to RH. We acknowledge the paucity of data underpinning this recommendation: this is a pragmatic strategy to minimise treatment interruptions due to medicine stockouts.

Provinces are encouraged to obtain limited quantities of Rifapentine 150mg single-drug formulation from the donated stock available at the Cape Medical Depot. For further information, please contact Ms. Moeng at [Helimamy.Moeng@westerncape.gov.za](mailto:Helimamy.Moeng@westerncape.gov.za).

It is anticipated that the current stock challenge concerning rifampicin-based combinations will be resolved by May 2025. A request for quotation of additional stock of rifapentine 150mg single drug formulation is currently underway.

**1. Substitution plan**

*(Guidance provided with credit and thanks to the Western Cape Department of Health and Wellness and the University of Cape Town: Medicines Information Centre).*

- RH must be substituted with rifapentine in combination with isoniazid, as per dosing guidelines provided in Annexure 1.
- Exclusions:
  - Children <12 years and < 38kg
  - Pregnant and breastfeeding women

<b>Available stock of RH should be reserved for children &lt;12 years and &lt; 38kg; and pregnant or breastfeeding women</b>
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**2. Patient management while on rifapentine and isoniazid**

- **Monitoring and management:**
  - Patients should be monitored for adverse events which should be reported as per normal processes.
  - There are no changes to the clinical management of the patient.
- **Patient outcomes:** No changes to how patient outcomes are assigned.
- **Drug Interactions:**
  - Like rifampicin, rifapentine is a potent inducer of drug-metabolising enzymes. Drug interactions with rifapentine are expected to be similar to rifampicin, and dosage adjustments of other concomitant therapies should be maintained as for rifampicin.
  - Refer to Annexure 2 for specific guidance on managing drug interactions with anti-retroviral treatment, contraceptives and antiepileptics. Please check for any drug interactions that might have been missed at TB-treatment initiation (Note that the table is not exhaustive, and clinicians should contact Medicines Information Centre (MIC) about interactions with other drugs as there are many others).
- **Course of therapy:** patients started or switched to continuation phase with rifapentine to remain on rifapentine until RH supply has stabilised.

**Procurement of rifapentine and Isoniazid tablets**

NSN	Product	Supplier	Contract
181879044	Isoniazid 100mg	Macleods Pharmaceuticals SA (Pty) Ltd	HP01-2023TB
181879045	Isoniazid 300mg	Viartis Healthcare (Pty) Ltd Pharma-Q (Pty) Ltd	HP01-2023TB
189710391	Rifampicin 150mg	Sandoz SA (Pty) Ltd	HP01-2023TB
181879049	Rifampicin, Isoniazid; 60mg, 60mg Tablet; 56 Tablets	Sandoz SA (Pty) Ltd Macleods Pharmaceuticals SA (Pty) Ltd	HP01-2023TB
181879047	Rifampicin, Isoniazid; 60mg, 60mg Tablet; 28 Tablets	Macleods Pharmaceuticals SA (Pty) Ltd	HP01-2023TB
222000932	Rifampicin, Isoniazid; 75mg, 50mg	Macleods Pharmaceuticals SA (Pty) Ltd	HP01-2023TB
181817633	Rifampicin, Isoniazid; 150mg, 75mg; Tablet; 56 Tablets	Macleods Pharmaceuticals SA (Pty) Ltd	HP01-2023TB
181817634	Rifampicin, Isoniazid; 150mg, 75mg; Tablet; 84 Tablets	Macleods Pharmaceuticals SA (Pty) Ltd	HP01-2023TB
181817575	Rifampicin, Isoniazid; 300mg, 150mg; Tablet	Macleods Pharmaceuticals SA (Pty) Ltd	HP01-2023TB
222000931	Rifapentine 150mg	To be obtained from the Cape Medical depot	

**NOTE: Please note that the doses contained in the fixed-dose formulations of Rifapentine/Isoniazid (300/300) currently available on contract are not suitable for the substitution plan proposed above.**

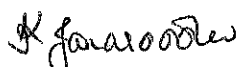
Updates on the supply of RH will be communicated when stock becomes available.

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**Circular dissemination**

Provinces and Healthcare Facilities are requested to distribute and communicate this information in consultation with the Pharmaceutical and Therapeutics Committees and all other relevant stakeholders.

Kind regards



**MS K JAMALOODIEN**  
**CHIEF DIRECTOR: SECTOR-WIDE PROCUREMENT**  
**DATE: 6/3/2025**

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Annexure 1: Interim guidance for RH-stock shortages for patients with drug-sensitive TB

**INTERIM GUIDANCE FOR RIFAMPICIN AND ISONIAZID (RH) FIXED DOSE COMBINATION STOCK SHORTAGES IN DRUG-SENSITIVE TUBERCULOSIS**



**(for children  $\geq 12$  years and  $\geq 38$  kg and adults, excluding children with TBM or miliary TB and pregnant or breastfeeding women)**

**Note:** The recommendation for the use of rifapentine in combination with isoniazid for the continuation phase of DS-TB treatment is based on very limited evidence and is mainly guided by expert opinion. This option should only be considered when RH FDC is not available. Any suspected adverse drug reaction(s) should be reported using the WC ADR Reporting Form or online using Sinjani. If you need further assistance, phone the MIC at 0800 212 506.

**Individual rifapentine and isoniazid products – dosing guidance:**

CONTINUATION PHASE			
Formulation	Rifapentine 150mg tab (daily)	+	Isoniazid (H) 100mg OR 300mg tab (daily)
Weight			
30-39kg	4 tabs	+	2 x 100mg tabs
$\geq 40$ kg	6 tabs	+	1 x 300mg tab

ADR=adverse drug reaction; DS = drug-susceptible; FDC = fixed dose combination; H = isoniazid; R = rifampicin; tab = tablet; TBM = TB meningitis; WC = Western Cape



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**Annexure 2. Guidance for management of common drug interactions with rifapentine**

**Please note:** Rifampicin and rifapentine are both strong enzyme inducers, and therefore interact with a large number of medicines. The inducing effect of rifampicin/rifapentine is expected to last for up to 2 weeks after stopping rifampicin/rifapentine. Remember to reduce the increased doses of the interacting medicine 2 weeks after discontinuing rifampicin/rifapentine. Always check for drug interactions. If you need assistance, phone the Medicines Information Centre at 0800 212 506 or send a WhatsApp to 071 840 1572.

<b>INTERACTING MEDICINE</b>	<b>EFFECT OF CO-ADMINISTRATION</b>	<b>MANAGEMENT</b>
Dolutegravir (DTG)	↓ DTG	Patients on DTG should have their DTG-containing regimen boosted to DTG 50mg 12-hourly. Continue DTG boosting until 2 weeks after rifapentine has been stopped.
Protease inhibitor (PI)- <b>Lopinavir/ritonavir (LPV/r)</b>	↓ LPV/r	Patients on LPV/r and rifapentine concomitantly should be on double dose of LPV/r (800/200 mg twice a day). ALT should be monitored monthly while on double dose. Continue double dose LPV/r until 2 weeks after rifapentine has been stopped. Discuss with ID specialist to see whether patient could be switched to dolutegravir - this would be preferable to double-dose LPV/r if possible.
Protease inhibitor (PI) – <b>Atazanavir/ritonavir (ATV/r) or Darunavir/ritonavir (DRV/r)</b>	↓ ATV/r	Avoid ATV/r or DRV/r in combination with rifapentine. Use rifabutin instead of rifapentine, in combination with the other anti-tuberculosis medicines.
Combined Oral Contraceptive (COC), Progestogen only oral contraceptive, Emergency	Potential ↓ contraceptive efficacy	Additional non-hormonal/barrier contraception must be used during and for 2 weeks after rifapentine treatment cessation.  Injectable contraceptives (Medroxyprogesterone acetate or

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contraception, Etonogestrel subdermal Implant		Norethisterone) may be used for patients on rifapentine.
Antiepileptics: Carbamazepine, Phenytoin, Valproic acid	<p>↑ Carbamazepine</p> <p>↓ OR ↑ Phenytoin</p> <p>↓ Valproic Acid</p>	Therapeutic drug monitoring required for carbamazepine, phenytoin & valproic acid, & dose adjustments required where necessary. Alternatively, lamotrigine or levetiracetam may be used.