Programmatic insights and practical strategies to drive uptake and embed 3HP effectively into routine TB prevention services

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05 August 2026

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Presentation Outline

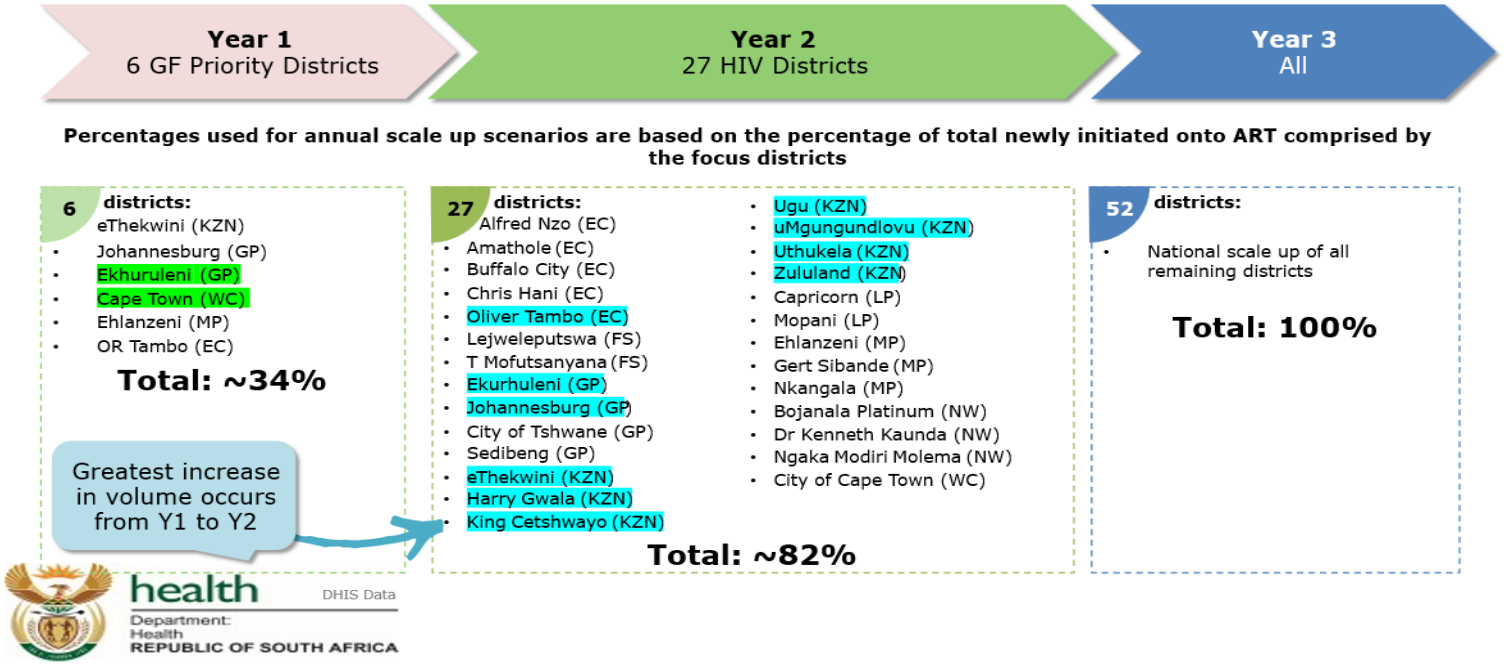
- Background
- Lessons learnt
- Progress so far
- Strategies for strengthening implementation
- Conclusion

Backgound

- WHO recommendation on the use of shorter regimen for TPT (2018)
- Implementation as part of IMPAACT4TB with funding from UNITAID
  - Placement of two staff at national level (HIV and TB Clusters) to provide TA and project manage the implementation of 3HP
- One global supplier of Rifapentine with limited manufacturing capacity
  - Rifapentine stock supply was initially limited to 1million packs for SA, then 600 000 and later ~450 000
  - Suppliers of INH on contract
- National scale up of 3HP was not feasible due to limited supply.
- Decision taken phase implementation over a period of 3 years whilst mobilising resources for scale up, project plan developed based on this

Background

- $15M awarded by GF for 3HP procurement, funding was to cover 2%, 4% and 6% of estimated national need in years 1, 2 and 3 respectively.



Implementation Plan (1)

- 6 GF supported districts were identified for the initial roll out
- GF SRs in these districts to provide technical support
- Target population:
  - PLHIV stable on ART eligible who are switching from TEE to TLD
  - ART naïve PLHIV in whom TLD is contra indicated
  - TB household contacts
  - Patients and those with silicosis
- Engagements and Capacity building
  - District Health Management Teams buy-in and joint planning
  - Training materials developed and training conducted - virtual training sessions
  - Interim Clinical guide, patient counselling guide and IEC materials

Implementation Plan (2)

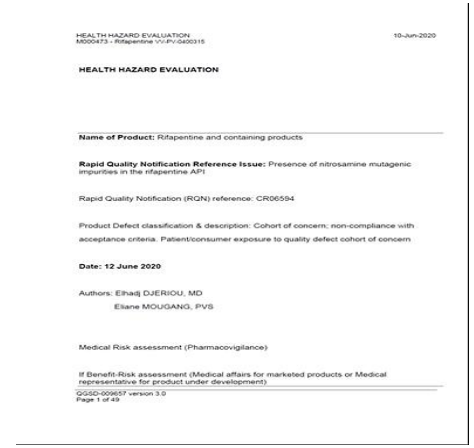
- Rifapentine procurement and distribution
  - ~60 000 packs of Rifapentine distributed to the 4 provinces
  - Repackaging at depot or hospital level
  - Monitoring stock levels
- Data Management , Monitoring & Evaluation
  - Revision of data collection tools
  - Information systems upgrades (e.g. DHIS, TIER) explored
  - Engagements on Pharmacovigilance system

Stakeholder and Partner engagement

	ROLES
Technical Partners	• Develop district specific 3HP scale up plans jointly with District Health Management Teams
	• Train clinicians on clinical management of patients on 3HP • Training of data capturers on capturing TPT information in TIER.Net
	• Supervision of staff at facility level • Ensure availability of job aids, desk references etc.
	• Pilot digital adherence tools for patients
	• Implement targeted innovative demand creation activities in districts with the lowest TPT initiation and completion rates.
Civil Society	• Implement targeted innovative demand creation activities in districts with the lowest TPT initiation and completion rates. – Social mobilisation – Community engagement • Advocacy for price reduction and FDCs

Some challenges along the way

- Packaging not ideal for dispensing which could result in wastage
- There were delays in Rifapentine production and delivery by Sanofi because of the Covid-19 lockdown
- Quality problem reported by the manufacturer
  - High levels of a contaminant - nitrosamines detected at factory
  - Concern about the carcinogenic effect of the nitrosamines



HEALTH HAZARD EVALUATION

10-Jun-2020

HEALTH HAZARD EVALUATION

Name of Product: Rifapentine and containing products

Rapid Quality Notification Reference Issue: Presence of nitrosamine mutagenic impurities in the rifapentine API

Rapid Quality Notification (RQN) reference: CR06594

Product Defect classification & description: Cohort of concern; non-compliance with acceptance criteria. Patient/consumer exposure to quality defect cohort of concern

Date: 12 June 2020

Authors: Elhadj DJERIOU, MD
Eliane MOUGANG, PVS

Medical Risk assessment (Pharmacovigilance)

If Benefit-Risk assessment (Medical affairs for marketed products or Medical representative for product under development)

SANOFI

Executive Summary Shortage

15 June 2020

ANTICIPATED RISK OF SHORTAGE OF

PRIFTIN (INN RIFAPENTINE) 150MG film-coated tablet

1 INTRODUCTION

This document describes the anticipated shortage of PRIFTIN 150MG film-coated tablet delivery from the current manufacturer Sanofi ANAGNI site located in Italy.

2 PRODUCT /MARKET INFORMATIONS

2.1 PRODUCT INFORMATION

Product name (local/international trademark)	PRIFTIN
INN/API/Antigen/Active ingredient	RIFAPENTINE
Dosage form/dosage strength/ presentation	150MG film-coated tablets Alu/Alu blister
Therapeutic indication	Antibiotic used in the treatment of pulmonary tuberculosis with specific indication for latent Tuberculosis
Status of the product/Comments	NA
Presentations and registration countries	Countries registered and marketed: South Africa (clinical studies: South Africa)

SAHPRA
South African Health Products Regulatory Authority

CSIR Campus
Building 10F
Meiring Naude Road
Brummeria
Pretoria

Date: 12/10/2020

The Responsible Pharmacist
Sanofi-Aventis SA (Pty) Ltd

Private Bag X207,

Midrand,1685

Gauteng

Subject: Priftin 150mg FC Tablets Contamination with Nitrosamine, 1-Cyclopentyl-nitrosopiperazine

Dear Mr James Graeme

Sanofi SA reported a quality defect of Priftin (Rifapentine) 150 mg Film-Coated Tablets to SAHPRA, that the product was contaminated with 1-Cyclopentyl-nitrosopiperazine (nitrosamine impurity).

There were four (4) batches (b/n; 9J252, 0J001, 0J1071 & 9J2361) of this Priftin 150 mg FC Tablet that were supplied to the National Department of Health; the product is currently stored at four of the Government Depots in SA.

The Priftin150 mg FC Tablets supplied to NDoH contains a nitrosamine impurity that has mutagenic carcinogenic properties and this nitrosamine impurity was present in the active pharmaceutical ingredient that was used in the manufacturing of the affected batches.

The active pharmaceutical ingredient manufacturer (Sanofi Brindisi, Italy) and the finished product manufacturer (Sanofi Anagni, Italy) both found the nitrosamine 1-Cyclopentyl-nitrosopiperazine to be above the acceptable 8.5 ppm specification.

SAHPRA received an update from Sanofi of the reviewed 1-Cyclopentyl-nitrosopiperazine specification from 8.5 ppm to 14 ppm. With the new revised specification three batches will be within 14 ppm and one batch will be rejected as it is above 14 ppm. The three batches that are within the specification, SAHPRA will note the decision that will be taken by Sanofi and monitor Sanofi's post-marketing surveillance reports in South African market if these batches will be used in the Latent TB Programme (3HP).

Kind regards

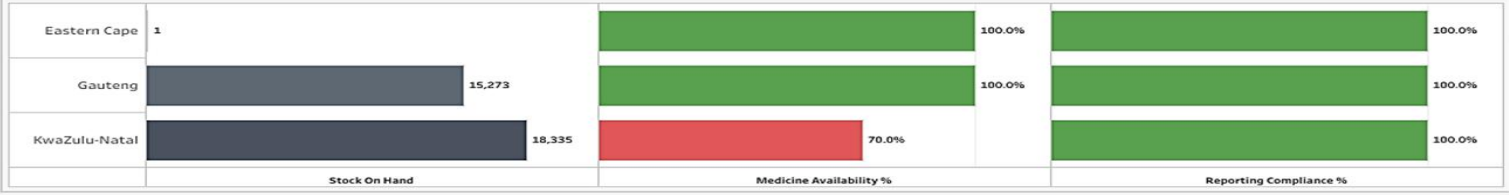
Mr Deon Poovan
Senior Manager: Inspectorate & Regulatory Compliance

Cc: Ms Portia Nkambule
Chief Operations Officer: South African Health Products Regulatory Authority

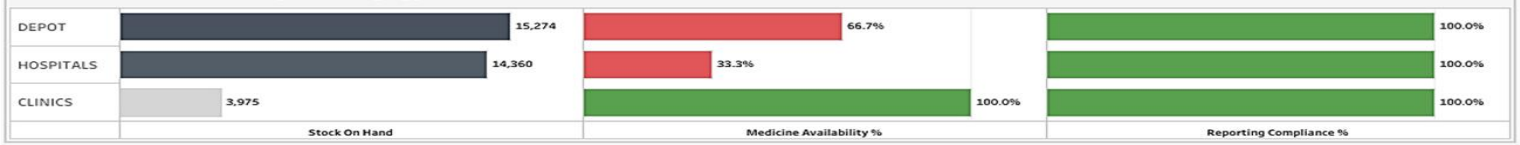
System for monitoring stock

Stock on Hand per Item Report

Total Stock on Hand per Province for:
Rifapentine 150 mg tablet, 24 tablets



Stock on Hand Information per Facility Type



Stock on Hand per Facility

Facility Name	District Name	Province Name	Last Update	Stock On Hand	Quantity on Order
Addington Hospital	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/22/2021	0	270
Cato Manor CHC	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/13/2021	3400	0
Hillbrow District Pharmacy	City of Johannesburg Metropolitan Municipality	Gauteng	9/21/2021	15273	0
Hlengisizwe CHC	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/17/2021	170	200
Inanda C CHC	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/17/2021	280	0
KZN Pharmaceutical Supply Depot	Null	KwaZulu-Natal	9/17/2021	0	3400
Mthatha Pharmaceutical Depot	Null	Eastern Cape	9/13/2021	1	0
Newtown A CHC	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/17/2021	85	0
Phoenix CHC	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/22/2021	15	0
Prince Mshiyeni Memorial Hospital	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/22/2021	14360	0
Tongaat CHC	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/22/2021	25	0
Wentworth Hospital	eThekwini Metropolitan Municipality	KwaZulu-Natal	9/22/2021	0	12

FILTERS & INFORMATION:

Province or District
Province

Select Province
All

Select District
All

Select Category
All

Select Item
Rifapentine 150 mg table..

Select Date Range
9/1/2021 to 9/30/2021

Legend: Medicine Availability

90-100%	
80-90%	
< 80%	

Legend: Reporting Compliance

80-100%	
< 80%	

Latest Data:
22-Sep-2021

Implementation

DISTRICT	APR-JUN 2021	JUL – SEPT 2021	OCT-DEC 2021	JAN -MAR 2022	APR – JUN 2022	JUL -SEPT 2022	OCT – DEC 2022	TOTAL
JHD		99	1352	2578	3239	3028	1209	**11 505**
ORT	484	2248	2505	2687	2066	1371	1561	**12 922**
Ehlanzeni		888	576	342	352	265	151	**2574**
eThekwini		863	1667	3040	1492	3922	3007	**13 991**
Ekurhuleni					461	1445	659	**2565**
TOTAL	**484**	**4098**	**6100**	**8647**	**7610**	**10031**	**6587**	**43 557**

- Data was manually compiled from TPT paper registers and reported directly to 3HP project manager at national level
  - not incorporated into the standard electronic system TIER.Net at end of life, no expected adjustments to include other TPT regimens/TPT module
  - Reporting outcomes currently not aligned to cohort monitoring
- Paper based method cumbersome, especially for high volume facilitiesPaper based method cumbersome, especially for high volume facilities

Implementation Challenges

Poor Uptake:

- Poor demand creation
- Initial implementation outside of standard treatment guidelines
- **Concerns about constrained supply of Rifapentine**

Stock Management

- No stock in 4 provinces (LP, FS, NW and NC)
- No Rifapentine delivered for over a year
- **Quality problems reported early 2023**
- Sanofi pulled out of supplying South Africa

Single-dose Formulations:

- **Pill burden as reported by patients**
- **Pre-packing of medicines labour intensive in pharmacies and depots**
  - lack of human resources for pre-packing
  - Lack of accountability for Rifapentine stock at depot level
- Insufficient space at the depots to stock large quantities

Supply constraints:

- **Administrative issues related to handling of Donation stock caused delays in getting RPT to facilities**
- **Inconsistent deliveries by the supplier**

How have we addressed these challenges?

- Guidelines on Treatment of TB Infection released in 2023
- FDC's registered by SAHPRA
- Rifapentine (singles and FDCs) included in TB contract ensuring a more reliable supply
- Provincial responsibility for procurement of medicines (Funding within Conditional Grant)
- TPT indicators on initiations and treatment outcomes included in DHIS
  - Cannot be disaggregated by regimen
- TPT Register developed, printed and disseminated to all provinces
- Inclusion in Standard Treatment Guidelines
- Pharmacovigilance system

Plans going forward

- Dissemination of the 3HP clinical Guide
- Explore innovative educational channels for demand creation
- Training on 3HP
  - WhatsApp training platform
  - Webinars
  - Virtual/Face to face training
- Other initiatives include the TB Calculator

Progress

INDICATOR : NUMBER OF HIV POSITIVE CLIENTS ON ART INITIATED ON TPT									
Province	Baseline (2024-25 Final perfomance)	2025-26							
		Annual BP Target	Q1 Final perfomance	Q2 Final perfomance	Q3 Final perfomance	Quarter 4 (Jan-March)			
						Q4 Target	Q4 Actual achieved	% Q4 Actual Achieved	Total ART clinets TPT start
EC	37 869	30 674	5 506	6 230	5 759	7 671	6 585	86%	24 080
FS	15 636	12 665	1 633	2 395	2 426	4 761	2 754	58%	9 208
GP	79 419	72 883	13 640	12 650	10 814	18 221	12 630	69%	49 734
KZN	74 657	60 472	13 105	11 766	9 896	16 144	11 171	69%	45 938
LIM	23 547	19 073	4 131	9 296	6 937	4 770	5 189	109%	25 553
MPU	26 551	21 506	5 164	5 380	5 090	5 376	5 553	103%	21 187
NC	4 390	3 556	583	609	513	889	652	73%	2 357
NW	13 207	10 698	5 350	5 578	4 838	2 675	5 297	198%	21 063
WC	16 313	13 214	1 830	3 344	2 713	3 304	2 482	75%	10 369
NATIONAL	**291 589**	**244 741**	**50 942**	**57 248**	**48 986**	**63 811**	**52 313**	**82%**	**209 489**

Progress

Province	TB contact 5 years and older start on TPT April 2025 - March 2026	TB contact under 5 years start on TPT April 2025 - March 2026	Total contacts on TPT
za South Africa	**64256**	**14788**	**79044**
ec Eastern Cape Province	12328	2173	14501
fs Free State Province	4045	533	4578
gp Gauteng Province	8693	1136	9829
kz KwaZulu-Natal Province	12620	3181	15801
lp Limpopo Province	2663	441	3104
mp Mpumalanga Province	3737	741	4478
nc Northern Cape Province	2842	568	3410
nw North West Province	4447	772	5219
wc Western Cape Province	12881	5243	18124

Progress

3HP 150	Quantities
Total stock on hand (depots and hospitals)	105 491 packs
Depots	104 491 packs
Quantities on order	20 packs

Low uptake of 3HP overall resulting in expiry on shelves and wastage

UNHLM Targets for TB

- Up to 45 million people treated for TB
- Up to 4.5 million children treated for TB
- Up to 1.5 million people treated for drug-resistant TB
- Up to 45 million people treated with TB preventive treatment, including:
  - 30 million household contacts, and
  - 15 million people living with HIV

SA Targets	2023	2024	2025	2026	2027	2023-2027
Contacts > 5yrs	128,810	120,003	144,992	152,741	149,519	696,065
Contacts under 5 yrs	30,934	29,710	33,187	34,135	32,720	160,686
PLHIV	465,806	618,841	671,392	684,888	688,521	3,129,447

Conclusion

- SA is lagging behind on targets and likely not to attain the UNHLM 2027 targets
- We need to prioritise prevention strategies – Treatment of TB infection is a quick win
- TB preventive treatment has been shown to be the most effective intervention to reduce the burden of TB disease.
- Scaling up treatment through screening of TB contacts, People living with HIV and other at risk groups will help us reach the end-TB strategy milestones and target

INTERIM CLINICAL GUIDANCE ON THE USE OF 3HP

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3HP DOSING CHART

3HP Recommended daily dosages

Drug	Dose	Maximum Dose/day
Isoniazid (H)	5 mg/kg	300 mg *
Rifapentine (R)	15 mg/kg	900 mg

* If 300 mg tablets are not available, use 100 mg

Dosing: Rifapentine and Isoniazid (3HP)

Body weight (kg)	Rifapentine	Isoniazid		Duration
	150 mg tablets (once weekly)	300 mg tablets (once weekly)	Or 100 mg tablets once weekly	
30 - 49.9	5	3	9	3 months
>50	6	3	9	3 months

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Things to do when taking 3HP

- Tell the nurse or doctor if you are taking other medication such as contraceptives, ARVs or chronic medication.
- If you see another nurse or doctor, be sure to tell them that you are being treated with 3HP for latent TB infection.
- Alcohol use is associated with an increased risk of liver damage when taking Isoniazid.
- You should discuss drinking alcohol with your health care worker.

How to store Your Pills?

- Keep the medicine at room temperature away from children.
- Keep the medicine in the original package.

For Women

- This medication may interfere with hormone-based birth control (including birth control pills, rings, and shots).
- When taking 3HP, non-hormonal barrier forms of birth control (condoms or diaphragms) should be used to avoid pregnancy.
- If you become pregnant, stop taking your medicine and speak with your doctor or nurse.

ALWAYS FOLLOW THE INSTRUCTIONS GIVEN TO YOU AT CLINIC!

ALWAYS FINISH YOUR TREATMENT!

IF YOU EXPERIENCE SIDE EFFECTS, ALWAYS TALK TO YOUR NURSE OR DOCTOR ABOUT THEM.

PATIENT INFORMATION

12-Dose Latent TB Treatment Information

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COUNSELLING GUIDE FOR LATENT TB INFECTION TREATMENT

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Thank you

Dosing Chart for HP 300mg/300mg

Weight	Number of tablets once weekly for 12 weeks
30 – 35	3
36 – 45	3
46 – 55	3
56 – 70	3
>70	3

HP fixed dose combination for children is not available yet