Quality Assurance (QA) for Health Products

QA Notice

IN Nº 2023-06 Version 1 - 06/Nov/2023	Information on stability issue and reminder of the importance of manufacturer's recommendation on environmental conditions during storage, transportation and distribution for **Rifapentine 150mg tabs manufactured by Sanofi, Italy.**

Addressees

- Through Health Product Management (HPM) specialists, all Principal Recipients (PR) reporting procurement of the impacted product financed by The Global Fund.
- Any procurer, buyer reporting procurement of the impacted product financed by The Global Fund.

Purpose

The Global Fund Quality Assurance and Compliance Team is issuing this QA Notice to share information on stability concerns of **Rifapentine 150mg tabs Sanofi** procured with the Global Fund funding following information received from the **manufacturer** and reminding on the importance of manufacturer's recommendations on environmental conditions during storage, transportation and distribution.

This notice is for internal and external dissemination and country teams are expected to communicate this information to their relevant stakeholders.

Identification of the product(s) and manufacturer

Name of Manufacturer	Sanofi S.p.A Via Valcanello 4, 03012, Anagni, Italy
Commercial / Brand Name(s)	Priftin 150 mg
Formulation	Rifapentine Tablet, Film-coated 150mg
Packaging & Pack size & Type	Blister, Alu/Alu 1 box, 3 blisters, 8 talets per blister
Batch(es)	Impacted batches: 1J4401, 1J7323 (currently marketed batches), and 9J2501 (expired batch), as well as the 14 batches representative of 1J4401 (1J2931, 1J2932, 1J2912, 1J2911, 1J3311, 1J3321, 1J4591, 1J7331, 1J7511, 1J7171, 1J7631, 1J8421, 1J3331 and 1J8431).
Manufacturing / Release Date	Batches produced and released from 2020

Background

The Global Fund Quality Assurance and Compliance Team has been informed by Sanofi of Out Of Specification (OOS) results for unknown single impurity during stability studies for the product stored under +30°C. Initial investigations have showed that the increasing trend of unknown single impurity has been noted since 2020 just in correspondence to the New API batches manufactured in June-July 2020.

No OOS value for unknown single impurity is currently reported for on-going stability batches for the product stored under +25°C.

Sanofi took immediate corrective actions by stopping production for the product to be stored under +25°C and the product to be stored under +30°C and putting on hold release of the product batches in stock.

Since May 2023, Sanofi decided to resume the production for markets with registered storage conditions of under +25°C, and to release the batches for these markets.

Batches of product stored under +30°C in stock at the manufacturing site and destined to markets remain under quarantine, until the root cause is identified.

WHO Prequalification Program confirmed that no additional action is deemed necessary for the batches that have been distributed.

Nature of defect(s)

Details of defect or problem.	Out Of Specification (OOS) results in stability for unknown single impurity during stability studies at 30°C
Is there any evidence or suspicion of a risk to public health?	A review from pharmacovigilance (PV) experts has been performed and two versions of Health Hazard Evaluation (HHE) per Sanofi considering South Africa, Indonesia, Thailand and Taiwan as impacted countries with the following conclusion: “the cumulative weighted evidence is insufficient to suggest that the OOS results for unidentified single impurity in the impacted batches of rifapentine (150 mg, film coated tablet) resulted in any harm to the patients or caused a change in the frequency or nature of reported adverse events.”
Extent of the problem (eg. No. of batches).	All batches of products manufactured with New API batches manufactured in June-July 2020. The Product that is currently procured by the Global Fund’s Pooled Procurement Mechanism (PPM) and The Global Drug

	Facility with registered conditions under +25°C has not been impacted. South Africa reported direct TGF financed procurement of the affected batches (1J2932, 1J2912, 1J2911, 1J3311, 1J3321, 1J4591, 1J7331, 1J7511, 1J7171, 1J7631, 1J8421, 1J3331) with registered conditions under +30°C.
Extent of distribution of the product / batch (es).	TBD
Number of patients potentially impacted	TBD

Action/Investigations taken

South Africa is the only country where affected batches of Rifapentine with registered storage conditions at +30°C have been procured with The Global Fund funding. The South African Health Products Regulatory Authority (SAHPRA) have been informed by Sanofi Aventis. As a result, supply of Rifapentine has been stopped and current orders have been cancelled pending investigation findings.

As production and release of Rifapentine destined to markets with registered storage conditions at +30°C have been put on hold by Sanofi, no other country should be affected.

Until the full resolution of the issue, The Global Fund Quality Assurance and Compliance Team does not recommend procurement of the Rifapentine with registered storage conditions of under +30°C.

However, for Rifapentine with registered storage conditions under +25°C for which procurement is still active, the Global Fund Quality Assurance and Compliance team is sharing some precautionary measures.

Next Steps

Based on the information available to date and until further notice, the following actions are recommended by the Global Fund Quality Assurance and Compliance Team for **Rifapentine 150mg manufactured by Sanofi** with registered storage conditions under +25°C **procured with the Global Fund funding:**

National Regulatory Authority (NRA)

PR must inform the NRA of the same. NRA may investigate the case and decide whether suspension and recall of the affected batches are needed in their territories. PR is expected to implement any decision made by the NRA.

Procurement Agent

To rigorously adhere to the storage conditions for the transport and storage of the product as stated on the labelling such as store under +25°C.

To closely monitor the temperature conditions during the storage and transportation of the product and to maintain records of data that confirm compliance with these conditions i.e. by using temperature data loggers.

Central & Regional warehouse and at health facility level

To rigorously adhere to the storage conditions for the transport and storage as stated on the product label such as under +25°C.

To closely monitor the temperature conditions during the storage and transportation of the product and to maintain records of available data that confirms compliance with these conditions i.e. in using temperature data loggers.

Users and/or Patients

Patients or users who have experienced any adverse reaction or unexpected side effect after use of the product should report to their healthcare provider who should provide advice and report the case to the authorities.

Contacts

This QA notice does require a specific written response from PRs. PRs should copy the Global Fund's Quality Assurance and Compliance Team of any correspondence regarding the matter for follow-up**.**

Please direct the respective answers and any questions about this matter to the technical contact listed below.

Organisation	**Name / Function**	**E-mail address**
Global Fund	Sandrine Cloëz, Quality Assurance Specialist	sandrine.cloez@theglobalfund.org
Global Drug Facility	Nigorsulton Muzafarova, Lead Product Quality Officer	nigorsultonm@stoptb.org