Quality Assurance (QA) for Health Products

QA Information Notice

IN Nº 2021-05 **Version:10Nov2021**	**Precautionary measures for products supplied by Agio Pharmaceuticals Ltd., India.**

Addressees

- All PRs through HPM specialist.
- Any person having products in stock (central store, pharmacies, retailer), in transit or under custom clearance.
- Any procurers, buyers with a pending order.

Purpose

The GF QA is issuing this information notice to provide recommendations and way forward to PRs regarding the procurement of Finished Pharmaceuticals Products (FPP) (including Pediatric Co-trimoxazole Oral Suspension 240 mg/5ml) manufactured by Agio Pharmaceuticals Ltd., India.

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	Agio Pharmaceuticals Ltd., India T – 81,82, M.I.D.C., Bhosari. Pune – 411 026
INN Name	Pediatric Co-trimoxazole
Pharmaceutical form	Oral Suspension
Strength	240 mg/5 ml
Packaging & Pack size	100ml bottle
Batch(es)	Multiple
Expiry Date	Multiple

Background

- On the 19th of October 2021, GF QA received information from its Procurement Service Agent (PSA), of a safety notification issued by one of their qualified wholesalers, concerning quality issue for Pediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100ml bottle manufactured by Agio Pharmaceuticals Ltd., India. The wholesaler recommended to stop distribution of the product and to quarantine the remaining stock.
- On the 1st of November 2021, GF QA received a second alert letter from one of its partners regarding a recommendation to suspend procurement of products manufactured by Agio Pharmaceuticals Ltd., India. Incident investigation activities demonstrated that testing results of the complaint samples did not meet product specifications for several characteristics, as per manufacturer's testing outcomes.
- As a result of the investigation, the wholesaler issued on the 5th of November a recall for all batches of the Pediatric Co-trimoxazole Oral Suspension 240 mg/5 ml, 100 ml bottle they had distributed (see annex 1). The wholesaler also communicated that they stopped procurement of all products manufactured by Agio Pharmaceuticals Ltd., India.

Nature of defect(s)

Details of defect or problem.	Out of Specification results concerning physicochemical characteristics and total bacterial count were reported independently for several batches of Pediatric Co-trimoxazole Oral Suspension 240 mg/5ml.
Is there any evidence or suspicion of a risk to public health?	No concrete evidence of risk for patient. But Potential decrease in efficacy and safety risk regarding the intended population (pediatric, HIV).
Extent of the problem (eg. how many batches).	More than 40 concerned batches have been reported by TGF PSA.
Extent of distribution of the product / batch (es).	Three countries initially concerned as procured by TGF (Armenia (PO2001711) / Benin (PO2001023) / Guatemala (PO2000727)) But potentially all countries receiving Agio products are concerned.
Number of patients potentially impacted	TBD
Other products potentially impacted	Because of the potential critical GMP deficiencies, all FPPs manufactured by Agio might be impacted.

Action/Investigations taken

- The PSA identified the countries that were impacted by the **Pediatric Co-trimoxazole Oral Suspension 240 mg/5ml** OOS, provided the list to GF QA and contacted the PRs of the concerned countries recommending to stop distribution of the product and to quarantine the remaining stock. The PSA is managing the recall requested by the wholesaler on the 5th of November for the three countries where PSA distributed this product.
- GF QA required the PSA to stop procuring any Pharmaceutical Finished Product manufactured by Agio India including Pediatric Co-trimoxazole Oral Suspension 240 mg/5ml.

Next Steps

The following additional actions are recommended by GF QA:

- To stop procuring any Finished Pharmaceutical Product manufactured by Agio including Pediatric Co-trimoxazole Oral Suspension 240 mg/5 ml and Aciclovir 200mg , dispersible, 100 tab, 10x10 blister;
- To stop any shipment and further distribution of any batches of Pediatric Co-trimoxazole Oral Suspension 240 mg/5 ml within the supply chain (wholesaler/regional or central distributors);
- To put in quarantine any batch of Pediatric Co-trimoxazole Oral Suspension 240 mg/5 ml at central storage level, regional as well at peripheral level (pharmacy and retail level) of the supply chain and assist the procurement agent of the PR with the recall of all the batches of Pediatric Co-trimoxazole Oral Suspension 240 mg/5 ml.
- Not to recall at user level;
- To report or confirm to the Procurement Agent copying GF QA the stock put in quarantine and to provide any additional information required for the recall of the batches;
- To contact and liaise on the same with National Regulatory Authority;
- In case patients have already taken this product, they need to contact their physician or pharmacist immediately.

Contacts

This IN requires a specific written response from the PR on Pediatric Co-trimoxazole Oral Suspension 240 mg/5 ml quarantine and recall.

PRs should copy GF QA Team on any correspondence regarding the quarantine and recall of the Pediatric Co-trimoxazole Oral Suspension 240 mg/5 ml quarantine manufactured by Agio.

Please direct the respective answers and any questions about this matter to the technical contacts listed below:

Organisation	**Name / Function**	**E-mail address**
Global Fund	Sandrine Cloëz, QA Pharmaceuticals Products Specialist	Sandrine.Cloez@theglobalfund.org

Annex 1: Wholesaler's recall Notification

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Imres BV
Larserpoortweg 26
8218 NK, Lelystad
The Netherlands
Tel.: +31 (0)320 29 69 69
CoC: Flevoland nr. 08023514
VAT-code: NL0085.51.601.B.01
www.imres.nl
info@imres.nl

URGENT Recall Notification

Subject: **Paediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100ml**

Manufacturer: **Agio Pharmaceuticals Ltd.**

5th November 2021

Dear customer,

Imres has become aware of a quality issue of the product Paediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100ml bottle, manufactured by Agio Pharmaceuticals Ltd. and distributed by Imres.
In follow up on the request to stop distribution of this product and to quarantine your remaining stock until further notice, we now have taken the decision to recall the product concerned.

Product: **Paediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100ml**

Manufacturer: **Agio Pharmaceuticals Ltd., Pune, India**

Batches: **All batches supplied through Imres (see attached list of batches)**

Background
Following a complaint on the discoloration of certain batches of the product, Imres has become aware that the concerned batches of the Paediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100 ml did not meet the specifications, after testing the complaint samples.
Testing of Imres retain samples did show out of specification results as well.
Therefore an initial recall was issued on these batches.

The nature of the out of specification result triggered Imres to do an investigation on the extent of the complaint and resulted in testing Imres retain samples of all batches of the product as well.
This resulted in many of the distributed batches showing out of specification results on microbiological purity (TAMC & TYMC).

As the out of specification results are shown in the vast majority of the retain samples, we have decided to do a recall of all batches of the product distributed.

Due to the outcome of the quality issue and the manufacturer not proceeding in further investigating the exact root cause, we have stopped the cooperation with Agio Pharmaceuticals Ltd.

To date no adverse events have been reported related to the recall.

Risk for patients who have already taken this product
In case patients have already taken this product, they need to contact their physician or pharmacist immediately.

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What you need to do

To assist us with this recall, please take the following steps immediately. Affected products can be identified by the batch number.

- Locate and immediately quarantine any affected products.
- Verify your physical stock by checking the cartons of Paediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100 ml with batch numbers mentioned on the attached list;
- Take all cartons of Paediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100 ml and batch numbers mentioned on the attached list out of your stock and quarantine them immediately for return or local destruction;
- Inform Imres with the outcome of this verification;
- If distributed to other organizations, inform them immediately of this defect and ask them to verify their stocks.
- Complete and return the attached Product Return Card to Imres BV when identified the affected products;
- After we have received your Product Return Card we will inform you on the next steps to be taken.

Please pass this information to all relevant persons in your institution. Additionally, please ensure that a copy of this letter is provided to any other organisation to which the affected batch has been transferred.

Thanks in advance for your kind cooperation and please accept our apologies for the inconvenience caused by this action.

If you should have any questions regarding this communication, please contact the following telephone number +31 (0)320 29 69 69.

Kind regards,

Mr. H.D. Kistemaker, pharmacist
QA Manager Imres BV

Attachments:

- List of Impacted batches
- Product Return Card

PRODUCT RETURN CARD FOR
Paediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100ml bottle

Please complete by checking the appropriate box below. Even if you have no inventory of listed batch numbers, please indicate this below and return this card by e-mail. If you currently have stock, complete the form noting quantity received and return this card immediately by email: info@imres.nl

Contact Name (please print)	Title	Signature and Date
Facility Name	Address	Phone Number

☐ We do not have any of the stock of Paediatric Co-trimoxazole Oral Suspension BP 240 mg/5 ml, 100ml bottle.
☐ We have the following stock (listed below) that we will be returning.
☐ We have the following stock (listed below) that we consider to destroy locally *.

Batch number	QUANTITY RECEIVED (number of bottles)	QUANTITY IN STOCK (number of bottles)	QUANTITY FOR RETURNING/DESTRUCTION (number of bottles)

Please do not return affected products without having made arrangements with IMRES BV.

* Before destroying the affected product locally, please contact IMRES at 00 31 320 296969 or info@imres.nl to discuss necessary proof of destruction.