Quality Assurance (QA) for Health Products

QA Notice

IN Nº 2022-03 Version 0 - 20/12/2022	**Temporary Suspension of procurement and delisting of pharmaceutical products which do not satisfy the criteria for authorization on Bioequivalence.**

Addressees

- All Principal Recipients (PRs) through Health Product Management (HPM) specialist.
- Any procurer, buyer.

Purpose

The GF QA is issuing this QA notice to inform of the delisting from TGF QA eligibility list of the following Pharmaceutical Products:

- Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg (Lupin Ltd.)
- Artemether/Lumefantrine Tablet, Dispersible 60mg/360mg (Guilin Pharmaceutical Co Ltd)
- Artemether/Lumefantrine Tablet 80mg/480mg (Guilin Pharmaceutical Co Ltd)
- Artemether/Lumefantrine Tablet 20mg/120mg (Guilin Pharmaceutical Co Ltd)
- Artemether/Lumefantrine Tablet, Dispersible 20mg/120mg (Guilin Pharmaceutical Co Ltd)
- Artemether/Lumefantrine Tablet, Dispersible 40mg/240mg (Guilin Pharmaceutical Co Ltd)

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 Manufacturers	Guilin Pharmaceutical Co Ltd, No 43 Qilidian Road, Guilin, Guangxi, 541 004, China (People's Republic of) Lupin Limited, Plot No. 6A1, 6A2, Sector-17, Special Economic Zone, MIHAN, Nagpur, Maharashtra, 441 108, India
Commercial / Brand Name(s)	NA
Formulation	- Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg (Lupin Ltd.)

	- Artemether/Lumefantrine Tablet, Dispersible 60mg/360mg (Guilin Pharmaceutical Co Ltd.) - Artemether/Lumefantrine Tablet 80mg/480mg (Guilin Pharmaceutical Co Ltd.) - Artemether/Lumefantrine Tablet 20mg/120mg (Guilin Pharmaceutical Co Ltd) - Artemether/Lumefantrine Tablet, Dispersible 20mg/120mg (Guilin Pharmaceutical Co Ltd) - Artemether/Lumefantrine Tablet, Dispersible 40mg/240mg (Guilin Pharmaceutical Co Ltd)
Packaging & Pack size & Type	All approved packaging and pack size
Batch(es)	NA
Manufacturing / Release Date	NA

Background

Global Fund Quality Assurance Team received the information from WHO-PQT that they have notified the Finished Pharmaceutical Products manufacturers Lupin Limited and Guilin Pharmaceutical Co Ltd. of the recommendation to suspend the products mentioned above.

This recommendation is justified by the observation of issues that have been considered of concern during bioequivalence inspection of the **CRO Accutest Research Laboratories (I) Pvt. and specifically the Clinical Unit of Unit I-A31, Mumbai, India**, over 30 May – 3 June 2022. A Notice of concern (NOC) has therefore been issued to the company and is published on WHO PQT website:

https://extranet.who.int/pqweb/inspection-services/noc-medicines

https://extranet.who.int/pqweb/news/noc-accutest-research-laboratories-india-published

The sponsors of the affected products i.e., Lupin Ltd. and Guilin Pharmaceutical Co Ltd are requested by WHO-PQT to review the impact of the **data integrity issues** raised on their respective studies and take action to confirm the bioequivalence and safety of their products. Their products will remain suspended and therefore delisted from TGF QA eligibility list until such a time as the required confirmations have been received and found acceptable by WHO-PQT.

At the time of the issue of this notice, the stated products were not delisted from the list of WHO prequalified products. A recall is not being considered at this time by WHO PQT.

Nature of defect(s)

Details of defect or problem.	WHO PQ suspension of 1 ARV manufactured by Lupin Ltd. and 5 antimalarial medicine formulations manufactured by Guilin Pharmaceutical Co Ltd following a NOC issued after bioequivalence inspection of the CRO **Accutest Research Laboratories** in charge of bioequivalence of the affected products.
Is there any evidence or suspicion of a risk to public health?	The findings made were mostly relating to the safety of the subjects that participated in those bioequivalence studies and to the integrity of the Bioequivalence data submitted. The above findings raised uncertainty on the bioavailability of the stated products with the comparators, but this should not be translated automatically in a failure of the generic formulation.
Extent of the problem (eg. nb batches).	No transaction reported in TGF Price & Quality Reporting (PQR) for the three affected products. However, some quantities of A/L disp, tab 20/120mg were allocated to Guilin for Nigeria and Tanzania but none of the products have been distributed yet. See detail of PO status annex1. • Nigeria (PPM): Products blocked at Guilin warehouse and quantities will be allocated to another supplier. • Tanzania (CPM): quantities have been dispatched to country (containers will arrive in Tanzania on December 22nd), Tridem Pharma Tanzania have informed the First Line Buyer (FLB) to freeze the goods in the warehouse upon arrival.
Extent of distribution of the product / batch (es).	According to TGF data the affected products have not been distributed and used to any country with TGF grant. (However, TGF current data should not be considered as fully exhaustive.)
Number of patients potentially impacted	No directly impacted patients.

Action/Investigations taken

- To inform internally in order to anticipate sourcing decisions.

Next Steps

Based on the information available to date and until further notice, the following actions are recommended by GF QA :

National Regulatory Authority

Therefore, national authorities should consider the content of the NOC and decide based on their own risk assessment to suspend the marketing authorization delivered based on WHO prequalification status and/or to decide whether recalls of the affected medicines are needed in their territories. Some of the medicines which have been recommended for suspension may be of critical importance (e.g. due to lack of available alternatives) in a given country. By consequence, the NRA can temporarily postpone the suspension in the interest of patients.

National authorities may also consider reviewing their decision concerning the market authorization of other products that have been granted based on bioequivalence study performed by the CRO Accutest Research Laboratories (I) Pvt. and specifically the Clinical Unit of Unit I-A31, Mumbai, India.

Procurement Agent

- To suspend the procurement by not putting any new order on the above affected products until further notice.
- To cancel existing order until further notice.

In Central & Regional warehouse and at health facility level

- It is not required to put the product in quarantine.

Users and/or Patients

- Patients should continue to take their medicines as prescribed and contact their doctors in case of questions or concerns.

Contacts

This QA notice does require specific written response from PR. PRs should copy GF QA 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

Annex 1: Order Status

PO No.	Product	Pack Size	Strength	Unit	QTY	Batch No.	MFG. Date	EXP. Date	Country	remarks
2022-004186, 0	AL Disp 20/120mg	6*1	20/120mg	BL	116,728	DL220803	2022/8/27	2024/8/26	Tanzania	CPM, dispatched with ETA on December 22.
PO2201636	AL Disp 20/120mg	6*30	20/120mg	Bl	467,850	DL220801	2022/8/15	2024/8/14	Nigeria	Block in Guilin warehouse
PO2201636	AL Disp 20/120mg	6*30	20/120mg	Bl	483,570	DL220802	2022/8/26	2024/8/25	Nigeria	Block in Guilin warehouse
PO2201636	AL Disp 20/120mg	6*30	20/120mg	Bl	145,260	DL220803	2022/8/27	2024/8/26	Nigeria	Block in Guilin warehouse
PO2201637	AL Disp 20/120mg	6*30	20/120mg	Bl	654,120				Nigeria	In production, INCO date on December 8.