Pharmacovigilance Newsletter

Quarter 2 ,Issue 2
December 2022

Causality assessment Workshop on COVID-19 vaccine safety data

An AEFI is any untoward medical occurrence (sign, abnormal laboratory finding, symptom, or illness) which follows immunization, and which does not necessarily have a causal relationship with the vaccination process or the vaccine itself.

A Causality assessment attempts to establish the level of certainty that the vaccine or the vaccination process was the origin or cause of the clinical picture and of the symptoms or signs observed in the vaccinated individual. Causality assessment of an Adverse Event Following Immunization/AEFI is thus a vital component of AEFI risk assessment, decision-making, and the initiation of action.

In Ethiopia, causality assessment of vaccines and medicines is conducted by the Pharmacovigilance advisory committee. The committee is composed of various high level health professionals with diverse specialty and has its own TOR to execute this important activity.

On November 22-23, a causality assessment was conducted on 7 cases of COVID-19 vaccines (Pfizer ,Janssen and Sinopharm), categorization was done based on the WHO electronic tool for AEFI causality analysis and recommendations were also provided for future prevention of SAE's . Of the seven cases categorized, four of the cases were found to be Vaccine product-related reaction (A1), one Immunization anxiety related reaction (A4) and two of the cases Coincidental (C).

As a way forward, the EFDA appreciated the effort done by USP/PQM+ in organizing the causality Assessment workshop and promised that the Pharmacovigilance team of EFDA will work on how to implement the recommendations given for an effective safety monitoring of vaccines. *(Attached are pictures of the event)*

This newsletter is prepared and shared quarterly by EFDA with the objective of providing Medicine safety information and sharing the activities of the pharmacovigilance center at EFDA to healthcare providers working at both the public and private sectors.

Inside this issue: Page

Activities Performed by the Pharmacovigilance center

Capacity building of the regional AEFI investigation task forces

The benefit of protection against a disease by immunization far outweighs the very small risks of immunization that might arise as a result of adverse event following use of vaccines. Despite the fact that such adverse events following immunization (AEFIs) are mostly mild and very rarely severe, measures still need to be put in place to monitor and prevent their occurrence and take appropriate regulatory action (s) on the products themselves if needed. The current system for monitoring drug safety (pharmacovigilance) is being coordinated by the Ethiopian Food and Drug Authority (EFDA) in collaboration with different stakeholders and partners.

Ethiopia has launched Covid-19 vaccination program on March 13/2021 throughout the country. After the vaccine introduction, AEFI reports have been collected by the pharmacovigilance team through active surveillance and spontaneous surveillance systems. After receiving the reports, careful investigation of serious AEFIs is critical. The ultimate goal of an investigation is to determine the likelihood of a causal link between a reported AEFI and the vaccine (s) administered or the vaccination process, or alternately to find another cause.

The AEFI investigation is being conducted by Regional AEFI Investigation Taskforce which is composed of different departments(EPI, Regulatory, PHEM and branch EFDA)within the respective regional health bureaus . However, there is a non-uniformity between the investigation capacity of the different Investigation taskforces. Delay in conducting investigation, incomplete investigation reports are some of the gaps observed.

Therefore, capacitating regional AEFI investigation taskforce members on how to properly conduct Investigation of Serious AEFI cases will Provide the necessary and appropriate information to the safety advisory committee. For this purpose, EFDA in collaboration with USP/PQMplus conducted a two day training and experience sharing event from November 17-18, 2022.

A total of 50 participants were trained at Hillside Hotel, Adama town on. The participants were AEFI investigation taskforce members from the following regions. Benshangul Gumuz, Afar, Gambella, Dire dawa, Amhara, Southwest Ethiopia, SNNP, Oromia, Sidama, Harari, Addis Ababa and Somalia. Experts from Federal Ministry of Health/EPI and Pharmacovigilance Experts from EFDA gave presentations on the selected topics. Power point presentations were used and each session was followed by discussion.

Standardized, presentations provided during the training were-Overview of the National Pharmacovigilance System, Overview of the National Immunization Program, Vaccines and basic concepts of AEFI, AEFI surveillance system in Ethiopia, Safety Surveillance of COVID-19 vaccines and country updates, Investigation of AEFIs and Causality Assessment, Actions and response to serious AEFIs, Vaccine risk communication. In addition, a case scenario was given to all participants to discuses the case and complete the AEFI investigation form. Groups presented how they investigated the case and read out how they completed the investigation form. It was discussed by the large group and inputs were given on the presentation from each group. Experience sharing on AEFI investigation from Amhara and SNNP regions and signing of The Terms of Reference for members of regional AEFI investigation taskforce was also another important activity conducted during the event. *(below are some picture of the event)*

Activities performed in the Pharmacovigilance center

Sensitization workshop on active TB drug-safety monitoring and management (aDSM)

Ethiopia has introduced aDSM as part of the introduction of new TB drugs and novel MDR TB regimens. The implementation of the intermediate package of aDSM and topics related to aDSM are included in the MDR TB management guidelines and training materials. To strengthen aDSM implementation regular discussions among the National TB Program (NTP), Armauer Hansen Research Institute (AHRI), the national Pharmacovigilance center (NPVC), and technical partners (especially the PAVIA project) is ongoing and coordinated support is being provided to Treatment initiating centers/TICs . Despite these efforts,the follow up of drug safety issues include detecting, managing and reporting of adverse events is not adequately practiced at most of the MDR TICs. There exists mainly negligence and skill gapin detecting and reporting o f ADEs related to the use of new TB drugs. Since there is no proper documentation and reporting of ADEs encountered, the overall burden of adversity directly attributable to anti-TB medicines is poorly quantified and it is not usually well profiled in individual TB control programmes. For this purpose, the sensitization programmes were planned.

Sensitization workshops on the implementation of active TB drug-safety monitoring and management (aDSM) were organized on March 29-30/2022 and March 30-April 01/2022 at Robi international and Eftah Hotel, Adama town. A total of (124) participants attended the events including 30TIC's, 12 regional TB programs focal persons, relevant staff members of Ethiopian Food and Drug Authority (EFDA), and focal persons of the national TB Program.

The workshops were officially opened by the Deputy Director of product safety directorate of EFDA, Mr. Teshita Shute. In his speech, he delivered a message on the rationale for active drug safety monitoring for new and repurposed TB drugs. He emphasized that activities on monitoring safety data of these drugs is inadequate and focal persons, especially from MDR TB TICs should be the main players in detecting and reporting those safety data.

During the workshop, presentations on relevant topics were provided with discussions with the participants. In addition, participants practiced on how to record and report data with the existing (paper-based) forms and the newly launched tools (Med safety mobile app and e-reporting).

During the general discussion, participants mainly raised issues related to the shortage of drugs such as RHZE, cycloserine, and the general supply system of TB medicines and ancillary medicines, and supportive supervision of TICs and investigation of the reported SAEs. Finally, reflections on issues raised were given by representatives from EFDA, NTP& EPSA, and general directions given by the representatives of the director of product safety directorate of EFDA W/ro Tigist Dires. She underscored that MDR TICs should focus on identifying and detecting of ADEs, especially for those of new and repurposed MDR TB drugs. She added the national PV center will provide the possible and needed support in this regard.

Some pictures of the programmes are attached below.

International safety update reports

Alert Summary: Medical Product Alert N°7/2022. Substandard (contaminated) paediatric liquid dosage medicines identified in WHO region of South-East Asia

This WHO Medical Product Alert refers to eight substandard products, identified in the WHO Region of South-East Asia. These products were identified in Indonesia and publicly reported by the national regulatory authority (Badan POM) on 20 and 30 October 2022. The eight products are Termorex syrup, Flurin DMP syrup, Unibebi Cough Syrup, Unibebi Demam Paracetamol Drops, Unibebi Demam Paracetamol Syrup, Paracetamol Drops, Paracetamol Syrup (mint) and Vipcol Syrup. (*Please see the table for further details.)*

These products contain unacceptable amounts of ethylene glycol and/or diethylene glycol as contaminants: this has been confirmed by laboratory analysis of samples by the authorities in Indonesia. To date, these products have been identified in Indonesia. They may however have marketing authorizations in other countries and may have been distributed, through informal markets, to other countries or regions.

Ethylene glycol and diethylene glycol are toxic to humans when consumed and can prove fatal. The substandard products referenced in the annex of this Alert are unsafe and their use, especially in children, may result in serious injury or death. Toxic effects can include abdominal pain, vomiting, diarrhea, inability to pass urine, headache, altered mental state and acute kidney injury which may lead to death.

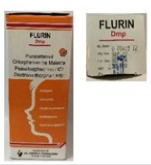
Advice to regulatory authorities, manufacturers, and the public

WHO requests increased surveillance and diligence within the supply chains of countries and regions likely to be affected by these products and they are advised to immediately notify WHO if these substandard products are discovered in their respective country. Increased surveillance of the informal/unregulated market is also advised.

Manufacturers of liquid dosage forms, especially syrups that contain excipients including propylene glycol, polyethylene glycol, sorbitol, and/or glycerin /glycerol, are urged to test for the presence of contaminants such as ethylene glycol and diethylene glycol before use in medicines.

If you have these substandard products, please DO NOT use them. If you, or someone you know, have used them or suffered any adverse reaction/event after use, please get medical treatment and report the incident to the National Regulatory Authority or National Pharmacovigilance Centre. *(Source: https://www.who.int/teams/regulation-prequalification/incidents-and-SF/full-list-of-who-medical-product-alerts)*

Ref. RPQ/REG/ISF/Alert N°7/2022: products contaminated with ethylene glycol and/or diethylene glycol
Annex 1 of 2

Product Name	TERMOREX	FLURIN DMP	UNIBEBI COUGH SYRUP	UNIBEBI DEMAM PARACETAMOL DROPS
Reported active ingredients	Paracetamol	Paracetamol, Pseudoephedrine HCl, Dextromethorphan HBr, Chlorpheniramine Maleate	Paracetamol, Guaifenesin, Chlorphenamine Maleate	Paracetamol
Stated manufacturer	PT Konimex	PT Yarindo Farmatama	PT Universal Pharmaceutical Industries	PT Universal Pharmaceutical Industries
Batch number	AUG22A06	All batches	All batches	All batches
Mfg. date	AUG 2022	N/A	N/A	N/A
Exp. date	AUG 2025	N/A	N/A	N/A
Packaging language	Bahasa Indonesia	Bahasa Indonesia	Bahasa Indonesia	Bahasa Indonesia
Available photograph				

Ref. RPQ/REG/ISF/Alert N°7/2022: products contaminated with ethylene glycol and/or diethylene glycol
Annex 2 of 2

Product Name	UNIBEBI DEMAM PARACETAMOL SYRUP	PARACETAMOL DROPS	PARACETAMOL SYRUP *(mint)*	VIPCOL SYRUP
Reported active ingredients	Paracetamol	Paracetamol	Paracetamol	Paracetamol, Guaifenesin, Chlorphenamine Maleate
Stated manufacturer	PT Universal Pharmaceutical Industries	PT Afi Farma	PT Afi Farma	PT Afi Farma
Batch number	All batches	All batches	All batches	All batches
Mfg. date	N/A	N/A	N/A	N/A
Exp. date	N/A	N/A	N/A	N/A
Packaging language	Bahasa Indonesia	Bahasa Indonesia	Bahasa Indonesia	Bahasa Indonesia
Available photograph