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ETHIOPIAN FOOD & DRUG AUTHORITY

Pharmacovigilance Newsletter

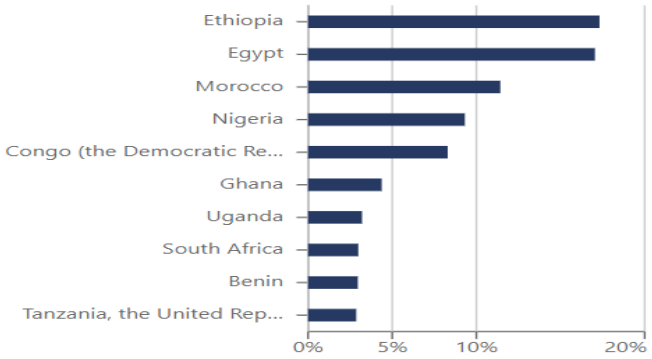
Quarter 2, Issue 1

January 2024

Ethiopia Ranked First in Africa by Sharing Adverse Events Following Immunization Data to the Global Database/VigiBase

Monitoring of adverse events following immunization (AEFI) is an essential strategy for ensuring the safety of vaccines. Post-licensure safety surveillance relies on the detection and reporting of AEFI. Reports on AEFI received at the national pharmacovigilance centre are verified for completeness and then data is shared to the global data base (VigiBase)which is the WHO global database of individual case safety reports (ICSR). The recent data on VigiBase, showed that Ethiopia ranked first in reporting higher number of suspected AEFIs followed by Egypt and Morocco in Africa.

An increased AEFI reporting allows the regulatory authority to detect rare adverse effects and potential safety signals early and consider regulatory actions. It also indicates the effectiveness of the implemented AEFI surveillance system. Moreover it enhances safety information sharing globally that will facilitates collective understanding of vaccine safety and support coordinated responses to emerging issues.



(https://vigilyze.who-umc.org, accessed on January 2, 2024)

EFDA Conducted Pharmacovigilance Stakeholders Meeting

The engagement of different stakeholders is pivotal for building a robust and responsive PV system. It promotes a collaborative and proactive approach to monitor medicine safety, and to protect the public health. For such reason, EFDA established a national PV stakeholder's forum in March 2023 that plays a crucial role in facilitating collaborative action. As per the ToR, the PV stakeholder's meeting was conducted on October 19, 2023 at Adama, Ethiopia for the second time.

The meeting had 31 representatives from various organizations, including Ministry of Health, regional health bureaus, regional regulatory bodies, professional associations, patient associations, private health facilities associations, market authorization holders (MAHs), Universities, different hospitals. In the meeting, updates on performed PV activities from the EFDA were presented and thorough discussions and reflections on the updates were held. Stakeholders identified the possible PV related activities that they will conduct in their respective institutions and planned for the next quarter.

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 to healthcare providers

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Activities Performed by the Pharmacovigilance Center

Hospital-Based Sentinel Surveillance for Adverse Events of Special Interest for vaccines

Hospital-Based Sentinel Surveillance (HBSS) for Adverse Events of Special Interest (AESI) for vaccine is a project intended to generate evidence on country-level background rates for AESI that could serve as a comparator for observed rare of AEFIs in the future vaccine introduction. AEFI data collected eventually support national and global vaccine safety monitoring. This project is implemented jointly with the Ohio State University Global One Health Initiative (GOHi) at Tikur Anbessa Specialized Hospital in 2022 and recently added Yekatit 12 Hospital.

Training for HBSS surveillance officers and data clerks was provided on the implementation protocol including data collection tools and national AESI system. Following the training, the team started collection from the two hospitals and the evidence generated from the project will help the EFDA to take appropriate corrective and prevention measures towards vaccine safety.

Vaccine Safety and AEFI Monitoring Training at Different Regions of Ethiopia

Ethiopian Food and Drug Authority in collaboration with regional health bureaus and Global Health Supply Chain_Procurment and Supply Management (GHSC_PSM) project provided capacity building training on vaccine safety monitoring and adverse events following immunization, for 120 health professionals (60 from each) from Afar and Tigray regions. The trainees were from Regional Health Bureaus and or regulatory, Woreda health office, Hospitals and Health Centers. The training was given for 3 days and conducted in each region in different time. . Participants shared their feedbacks on the training, identified obstacles, and discussion was held about the next steps in vaccine safety and AEFI monitoring. The regional regulatory director, EPI department Head, and an EFDA representative were present to address participant inquiries. Overall, the training sessions were successful, resulting in a significant improvement in trainees' awareness about AEFI monitoring and helps them to understand their role and duty in enhancing vaccine safety and AEFI monitoring.

In addition to healthcare professional capacity building, revitalization and refresher trainings on AEFI monitoring and investigation were given for all regional task forces. A total of 84 members of the taskforce, five from each regions, attended the training at Adama, Shashemene and Harar. Challenges regarding investigation of serious adverse events were discussed and possible recommendations mentioned by participants and future actions were stated by officials from EFDA.

Activities performed in the Pharmacovigilance center

Safety Profile of SinoPharm, Dolutegravir, Delamanid, and Bedaquiline in the Ethiopian Population

Pharmacovigilance systems are designed to monitor and assess the safety of medicines, including vaccine after they have been marketed and used by the larger population. These systems aim to detect, evaluate, and respond to adverse events (AEs) and other safety-related issues. For the routine safety monitoring EFDA mainly uses a spontaneous reporting system but when a new medicine is introduced in Ethiopia or the medicine's risk-benefit profile is of particular interest active surveillance will be implemented.

Active Safety Surveillance of SinoPharm COVID-19 Vaccine in Selected Health Facilities, Ethiopia.

The Coronavirus pandemic, declared a global health crisis by the WHO in March 2020, which necessitated the rapid development and deployment of vaccines to combat its spread. The SinoPharm COVID-19 vaccine was granted emergency approval by the Ethiopian Food and Drug Authority (EFDA) to be used in Ethiopia. Following its introduction active surveillance was conducted to determine the occurrence of adverse effects following immunization (AEFI), its incidence rate and the associated factors in Ethiopia. A multi-centric prospective observational study was conducted, involving adults (≥18 years) who received the SinoPharm COVID-19 vaccine at selected health facilities in six regions and two city administrations. Data was collected through direct observation at the vaccination site for 30 minutes and via phone calls on specific days after vaccination. During the call, participants were asked to report any AEFIs they experienced.

A total of 9,129 participants were included in the study and the overall incidence of AEFI was 26.2% (2,390). Of these, 0.6% (54 cases) experienced AEFI within 30 minutes of vaccine administration, while 25.9% (2,368 cases) experienced AEFI after 30 minutes. A total of 3,839 AEFI manifestations were reported, averaging 1.6 manifestations per participant. Among participants who reported AEFI, 58.3% (1,393 cases) experienced two or more manifestations. The most frequently reported AEFIs were injection site pain, headache, fever, arthralgia/joint pain, fatigue, chills, and nausea and/or vomiting. Participants of age between 30-39 years, being on medication, and having a history of substance use were significantly associated with the occurrence of AEFIs following SinoPharm COVID-19 vaccination.

Most of the AEFIs were non-serious, and this study indicated the benefits of Sinopharm COVID-19 vaccine in preventing serious and severe Covid-19 infections and mortality greatly outweigh the rare risk of adverse events. However, the EFDA will continue its safety monitoring.

Cohort Event Monitoring (CEM) of Dolutegravir (DTG) Containing ART Regimens in Selected Health Facilities of Addis Ababa, Ethiopia: an Interim Analysis

The introduction of DTG-based antiretroviral therapy (ART) has provided a potent treatment option for people living with HIV. However, the introduction of this regimen limited number of hyperglycemia, serious neurologic and neuropsychiatric adverse drug reactions (ADRs) were reported in different countries including Ethiopia. In Ethiopia, there was a lack of sufficient information about the safety of DTG-based regimens in the local population. To address this, the Ethiopian Food and Drug Authority (EFDA) conducted a cohort evaluation study on DTG-based regimens among patients receiving ART services in selected health facilities in Addis Ababa.

The study period was three years starting from April 2022 and each participant in the cohort was followed for 1 year starting from the enrolment date using phone calls and during routine care visits. The intended size of the cohort was 3000 patients to be followed for 12 months but in this interim data analysis, only 1294 patients were included and 330(22.5%) of them followed for one year. The Preliminary data analysis revealed that 10.9% of participants reported one or more adverse drug reactions (ADRs), headache (16.5%) and fatigue (14.6) are the most frequently reported ADRs. Most of the ADRs (47.2%) were classified as mild, and majority of ADRs (75%) occurred within the first 15 days of initiating DTG-based therapy. EFDA will communicate the final study findings after completion of the study.

Active Drug Safety Monitoring (aDSM) of Delamanid (Dlm) and Bedaquiline (Bdq) Containing anti-MDR TB Regimens in Ethiopia

The national TB program and EFDA have set active TB-drugs safety monitoring and management (aDSM) for the newly introduced anti-MDR-TB drugs, Delamanid (Dlm) and Bedaquiline (Bdq). This report therefore presented the description of the national ADR data received by EFDA between December 2021 to December 2023 from MDR-TB treatment initiation centers.

Of the total 293 patients who were reported to have ADRs, a total of 333 ADRs were identified which gives an average number of 1.14 ADRs per patient. The most common were peripheral neuropathy (60,18.0%), nausea and vomiting (49,14.7%), optic neuritis (32, 9.6%), Gastritis/dyspepsia (25, 7.5), drug-induced liver injury (DILI) (20, 6.0%), and Arthralgia/arthritis (24, 7.2%). Linezolid was the most suspected medicine for the ADR accounting for (87, 29.7%) of the ADRs reported, followed by cycloserine (23, 7.8%) and long-term regimen (LTR) (21, 7.2%). The majority of the reported cases were mild (135, 46.1%) and almost half of the reported ADRs 145(49.5%) were resolved. However, 3 (1.0%) of the cases were reported as life-threatening.

International Medicine Safety Updates

Safety Updates on Ranitidine Hydrochloride

Ranitidine is among the four histamine H2-receptor blockers first developed by Sir James Black in the early 1990s. Among the four H2 receptor blockers, Cimetidine 200mg/mL in 2mL ampoule injection and Ranitidine (as hydrochloride) 150 mg tablet, 25 mg/ ml in 2ml ampoule injection and Oral liquid 75 mg/5 ml are included in the Essential List of Medicine of Ethiopia (EML, 2020, Ethiopia). Ranitidine is also included in 'WHO Model List of Essential Medicines 23rd List, 2023 (WHO, Model EML 2023)'. Currently, the global experience showed that Ranitidine contains carcinogenic impurity called 'N-Nitrosodimethylamine (NDMA)' in Pharmaceuticals. In order to protect the health of the public, most of medicine regulatory authorities such as the European Medicine Agency (EMA), Medicine and Healthcare products Regulatory Agency (MHRA), and United States Food and Drug Administration (US FDA) banned ranitidine from their market.

In the interest of protecting the public safety and as many alternative medicines are available, the Ethiopian Food and Drug Authority (EFDA) passed the following decisions on the future use of ranitidine:

- ⇒ Suspension of the registration status of ranitidine in Ethiopia;
- ⇒ Withdrawal of ranitidine containing drugs from the essential medicine lists of Ethiopia,
- ⇒ Recall of all ranitidine containing products from the Ethiopian market

Safety Updates on Valproate

What are the valproate risks if taken during pregnancy?

Valproate use during pregnancy is harmful for the unborn child. Children exposed in utero to valproate have a high risk for:

- Congenital malformations,
- Neurodevelopmental disorders.

The risks are dose-related and there is no threshold dose below which no risk exists. Any dose of valproate during pregnancy can be harmful for the unborn child. The nature of the risks for children exposed to valproate during pregnancy is the same irrespective of the indication for which valproate has been prescribed. Both valproate monotherapy and valproate polytherapy including other antiepileptics, are frequently associated with abnormal pregnancy outcomes.

Key information to remember: Contraception and Pregnancy

Valproate is an effective medicine for epilepsy and bipolar disorder. Valproate should not be taken by women or girls (of any age) unless nothing else works. This is because valproate can seriously harm an unborn child when taken during pregnancy.

If you are taking valproate and are able to become pregnant:

- o Always use effective contraception (birth control).
- o Do not stop using the contraception at any time.

If you are thinking about having a baby:

- o Speak first to your doctor before stopping your contraception.
- o Never stop taking valproate unless your doctor tells you because your condition may become worse.

If you are taking valproate and have become pregnant:

- o Do not stop taking valproate: this is because your epilepsy or bipolar disorder may become worse.
- o Talk promptly to your doctor about your options and what you need to know. Your doctor will explain if you need to switch to another treatment and how.

Paternal exposure to valproate

Safety Information Letter was submitted to Ethiopian Food and Drug Authority (EFDA) relating to the label update and to additional Risk Minimization Measures (aRMMs) proposed by Sanofi (Marketing Authorization Holder for Valproate) to reflect the results of the Post-Authorization Safety Study (PASS) Paternal exposure (CCDS V36). The PASS Paternal exposure is a retrospective observational study using electronic medical records from three European Nordic countries, namely, Sweden, Denmark and Norway. Based on the results of this PASS Paternal exposure, Sanofi considered that a potential risk of neurodevelopmental disorders after paternal exposure to valproate at the time of conception in comparison to lamotrigine and levetiracetam.

Therefore, Sanofi submitted a label update as well as aRMMs, including a Direct Healthcare Professional Communication (DHPC) to reflect the results of the PASS Paternal exposure. Those changes are currently being assessed by the Pharmacovigilance Risk Assessment Committee (PRAC) in the European Union (EU) and by other Health Authorities worldwide