PHARMACOVIGILANCE/POST MARKETING SURVEILLANCE NEWSLETTER

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Activities at the National Pharmacovigilance Centre in the Year 2018

Content

EDITOR'S NOTE...

We wish to thank all our numerous stakeholders who have been working tirelessly with the National Pharmacovigilance Centre (NPC) to ensure the safe use of medicines in Nigeria. The NPC is committed to sending out quarterly newsletter to its stakeholders. The objectives of the Newsletter are to disseminate information on Pharmacovigilance activities nationally and globally, to educate stakeholders on medicine safety issues, to promote rational use of drugs and to promote reporting of Adverse Drugs Reactions (ADRs). This edition of the newsletter brings you an update of activities at the National Pharmacovigilance Centre in the year 2018.

We encourage Health care Professionals and other stakeholders to continue to report all adverse drug reactions. Your valued comments and acknowledgement of receipt of this issue through our email addresses (nafdac_npc@yahoo.com; pharmacovigilance@nafdac.gov.ng, fdic@nafdac.gov.ng) would be most appreciated.

Thank you for your relentless efforts in strengthening Pharmacovigilance System in Nigeria.

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Text any DRUG RELATED PROBLEM to the SHORT CODE 20543 (For free on MTN, Glo, Etisalat and Airtel) for action by the Pharmacovigilance Centre.

Adverse Drug Reactions Reports Received In 2018

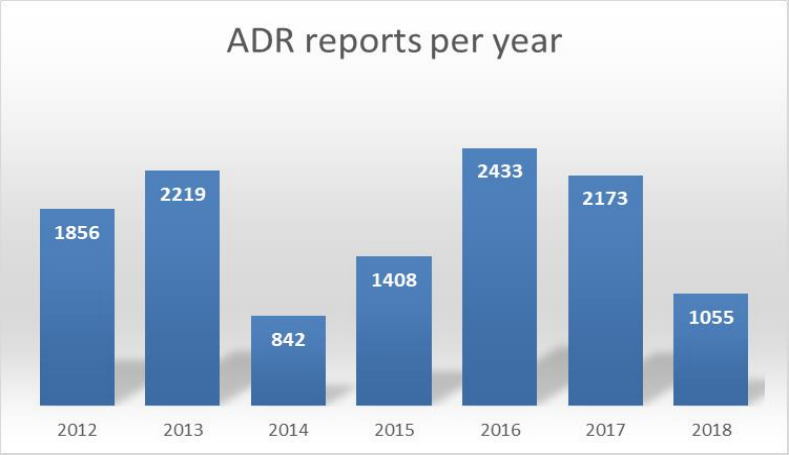
Currently, spontaneous reporting of ADRs remain the mainstay of Pharmacovigilance activities in Nigeria. Reporting of ADRs is an ethical responsibility of healthcare providers and a mandatory responsibility of Marketing Authorization holders. ADR reports are received as documented on the yellow forms from healthcare professionals and healthcare providers. Some MAHs submit ADR reports to the NPC using the Council of International Organization for Medical Sciences (CIOMS) forms. Adverse events following immunization (AEFI) are also received from the NPHCDA. These reports are termed Individual Case Safety Reports when they meet the minimum criteria for a valid ICSR. The minimum criteria include an identifiable reporter, a suspect product and an event or outcome. The issue of whether or not an ADR report forms an ICSR has been a major challenge, especially with regards to CIOMS forms. In 2018 for instance, none of the CIOMS forms received at the NPC could be transcribed into an ICSR because they did not meet the minimum criteria for a valid ICSR.

The National Pharmacovigilance Centre received A total of one thousand and fifty-five (1055) Reports of Adverse Drug Reactions (ADRs) from health professionals across the country from both private and public health institutions, MAH of Pharmaceutical products and the NPHCDA from January to December, 2018.

Table 1. breakdown of the ADR reports received at the NPC in 2018

Type of Report	Number of Reports
ADR (yellow) forms	666
(CIOMS) forms,	363
Adverse Events Following Immunization (AEFI) reporting forms	26
Total	1055

Figure 1. Number of reports submitted at the NPC by Healthcare professionals from 2012 to 2018



The NPC in Nigeria is a member of the WHO International Drug Monitoring Program. It is subscribed to the Vigiflow, an international database for ADR reports. ADR reports received at the NPC are

uploaded to the Vigiflow after thorough causality assessments by PV experts at the NPC. Therefore, ADR reports submitted to the NPC help to inform regulatory decisions that promote the safety of medicines not only locally but also contribute to improving Pharmacovigilance at the Global level.

Pharmacovigilance is our collective responsibility as MAH of pharmaceutical products, regulators, healthcare professionals, patients and the general public, we must therefore contribute each our quota to strengthen PV in the country and enhance the safety of medicines for patients.

Pharmacovigilance Africa (PAVIA) Project in Nigeria

PAVIA is a Coordination and Support Mechanism, targeted at improving responsible uptake of new drugs and vaccines by strengthening local capacity for Pharmacovigilance (PV) towards recognizing, reporting, and acting on untoward effects of such products.

It is funded by the European-Developing Countries Clinical Trials Partnership (EDCTP), a funding mechanism under the EU's Horizon 2020 research program that aims to evaluate, primarily through clinical trials, new products for poverty-related infectious diseases (PRDs) in sub-Saharan Africa and to build local capacity for clinical trials.

The PAVIA project aims to strengthen Pharmacovigilance (PV) in four African countries. The countries are Ethiopia, Nigeria, Swaziland and Tanzania. This will be achieved by coordinating and bringing together stakeholders and ongoing activities and initiatives in addition to direct support through training and technical assistance.

PAVIA's approach is based on the analysis that in these and other African countries, the capacity for PV is often weak due to a number of challenges. These challenges include:

- *Inefficient functional regulatory and organizational structures*
- *Unclear roles and responsibilities for stakeholders towards ensuring the safety of medicines*
- *Ineffective active surveillance of adverse reactions*
- *Disconnected databases and use of tooling for event detection, reporting, analysis and dissemination to relevant stakeholders*
- *Inadequate human resources*
- *Inadequate PV-relevant skills and competencies at various levels*
- *Limited experience in monitoring and steering performance of PV systems*

- *Insufficient alignment between regional and international initiatives.*

PAVIA's activities focus on cooperation and linkage between countries' regulatory authorities responsible for PV and Infectious Disease Control Programs responsible for introduction of new drugs and vaccines for PRDs.

The initial focus of PAVIA is on the introduction of new drugs and treatment regimens for multidrug-resistant tuberculosis (MDR-TB) by the National Tuberculosis Programs (NTPs).

The reason for choosing this focus is that these new treatments are being introduced despite limited safety data from clinical trials, and that in each of the project countries this introduction is being done in a unified manner according to WHO guidance, including for drug safety monitoring, under a single project. This project, Challenge TB, is funded by USAID and executed by the NTPs with technical support by one of PAVIA's partners, KNCV Tuberculosis Foundation.

PAVIA will in each country establish a "triangle" cooperation between the NTP, the regulatory authority and a local medical research institute (MRI) providing clinical expertise.

This "triangle" will provide a channel for reporting and interpreting safety signals in MDR-TB treatment, serve as a training ground for country PV staff and clinicians, and provide a demonstration project for similar linkages with other disease control programs.

The PAVIA project will be implemented in three phases; phase 1 starting with a project-wide supranational kick-off meeting with involvement of all consortium partners, selected international stakeholders and Advisory Board members.

The joint kick off meeting of PAVIA and PROFORMA took place in Dar El Salam, Tanzania from 30th April to 4th May, 2018. PAVIA and PROFORMA are two consortia funded by European-Developing Countries Clinical Trial Partnership.

In Nigeria, The National Agency for Food and Drug Administration and Control (NAFDAC), Institute of Human Virology Nigeria (IHVN), University of Benin (UniBEN), National Tuberculosis and Leprosy Control Programme (NTBLCP) and KNCV Tuberculosis Foundation Nigeria are participating in PAVIA project.

The Nigeria Country Specific Kick-Off Meeting and Baseline Assessment on Pharmacovigilance Africa (PAVIA) Project was held from 24th to 28th September, 2018 At KNCV Conference Hall, Abuja.

The Nigeria Country Specific meeting was targeted at co-ordinating and bringing together stakeholders relevant to the implementation of PAVIA project. The meeting also provided a platform to conduct a Baseline assessment of PV activities in Nigeria.

Director PV/PMS Making a Presentation on Nigeria Pharmacovigilance Network at Pavia Meeting

A total of 125 participants drawn from Government organizations, pharmaceutical industries, the academia, healthcare sector attended the kick-off meeting

Dissemination of Round Four (4) Survey on The Quality of Antimalarial Medicines in Nigeria at NAFDAC Central Laboratory, Oshodi, Lagos.

The National Agency for Food and Drug Administration and Control (NAFDAC) in collaboration with United State Pharmacopoeia (USP) conducted Round Four (4) Survey on the quality of anti-malarial medicines in Nigeria. Pharmacovigilance/Post Marketing Surveillance (PV/PMS) Directorate coordinated the survey on behalf of NAFDAC.

The report of the survey was presented to stakeholders dealing in regulated products at NAFDAC Central Laboratory, Oshodi, Lagos on 12th December 2018. The report was presented to inform stakeholders on the incidence of substandard anti-malaria medicine in Nigeria and solicit their support in the fight against the manufacture, distribution and sale of substandard anti-malaria medicines.

The result of the survey showed that:

- 727 Samples out of 741(98.1%) passed quality tests.
- 14 samples out of 741 (1.9%) failed quality testing, as they did not conform to specification.

The failed samples included 8 Artemether+Lumefantrine tablets, 1 Sulfadoxine Pyrimethamine tablets, 2 Quinine Sulfate tablets, 1 Artesunate+Amodiaquine tablet and 2 Others.

6 samples failed disintegration tests (42.9%); 3 samples failed assay, (21.4%); 4 Samples had low API (28.6%); One (1) product is not registered with NAFDAC and it has no Manufacturer's address (7.1%).

Table 3. Percentage Pass & Failure of Samples of antimalarial medicines

Lab result of sample	Number of samples	percentage
Fail	14	1.9
Pass	727	98.1
total	741	100

Table 4. Distribution of failed and Passed samples by zones

S/N	Geopolitical Zone	No of passed samples		No of failed samples		Total No of samples	
	Zone	Qty	%	Qty	%	Qty	%
1	North Central	143	97.3	4	2.7	147	100
2	North East	103	96.3	4	3.7	107	100
3	North West	131	100	0	0.0	131	100
4	South East	131	100	0	0.0	131	100
5	South South	127	95.5	6	4.5	133	100
6	South West	92	100	0	0.0	92	100
	Total	727	98.1	14	1.9	741	100

During the presentation of results, it was recommended that

Pharmacovigilance/Post Marketing Surveillance Directorate should sustain the mop up of failed samples to prevent exposure of the members of the Public to substandard and falsified antimalarial medicine.

Drug Evaluation and Research Directorate should strengthen monitoring of Good Manufacturing Practices of manufacturers of antimalarial medicines, especially the manufacturers of failed samples.

The Port Inspection Directorate should sustain the surveillance on imported antimalarial medicines to ensure that only good quality antimalarial medicines are imported into Nigeria.

NAFDAC Zonal and state officers should intensify the monitoring of distribution and retail outlets, especially in rural areas to ensure that antimalarial medicines are stored under suitable conditions.

Distributors, Wholesalers and retailers of medicines should ensure proper transportation and storage to ensure that quality of medicines is maintained along distribution chain.

Manufacturers and Marketing Authorization Holders

should ensure that their products are distributed and transported under suitable storage conditions along the distribution chain up to the retail level, to ensure that their quality are retained.

Programme Managers of Public Health Programmes should make adequate provision for quality assurance of medicines, especially antimalarial medicines.

Conclusion

The successful completion of the Round 4 Survey has laid a solid foundation for effective post marketing surveillance of antimalarial medicines. The report of Round 4 Survey revealed that 727 out of 741 samples of antimalarial medicines (98.1%) passed quality tests while 14 samples (1.9%) failed.

The failure rate of antimalarial medicine in Round 4 survey is 1.9% as against 1.6% in Round 3. There is need to strengthen NAFDAC's collaboration with PMI/USP, USAID, NMEP, NPSCMP & other relevant stakeholders to ensure that the level of substandard and falsified antimalarial medicines in Nigeria is reduced to the barest minimum.

Pharm. Ali Ibrahim Presenting the Round Four (4) MQM Report

Safety of Ketoconazole

Ketoconazole is an azole antifungal medication used primarily to treat fungal infections. The use of ketoconazole oral tablets has been restricted by some regulatory authorities due to potentially fatal liver injury, risk of drug interactions and adrenal gland problems

A search of the Nigerian National Pharmacovigilance Center (NPC) database revealed four cases where ketoconazole was reported either singly or along with other drugs as the suspect drug for the reported reactions. Reported adverse reactions included collapse after few minutes of oral administration of suspect drugs (2 cases), skin discolouration (1 case) and swollen parts of the body and mild to intense rashes that affected the left ear(1case).

The Concern over the safety of Ketoconazole oral tablets has been extensively deliberated on by the National Drug Safety Advisory committee (NDSAC). In view of this, NAFDAC implores healthcare providers to limit use of oral ketoconazole to cases where there are no safer alternatives and the benefits of its use outweighs the risks to the patient.