PHARMACOVIGILANCE/POST MARKETING SURVEILLANCE NEWSLETTER

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PHARMACOVIGILANCE: *A VIEW ON MEDICAL DEVICES*

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 the 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 focuses on **Pharmacovigilance:** *A view on medical devices*

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.

You may also send us an email if there are any areas of interest that you would want addressed in subsequent issues of the newsletter

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

Fraden Birtus fsi

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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

MED SAFETY APPLICATION

The Agency has adopted the Med Safety App (WEB-RADR) for improved ADR reporting in Nigeria.

The Med Safety App was developed through the Innovative Medicines Initiative WEB-RADR project sponsored by the WHO, WHO Programme for International Drug Monitoring (UMC) and Medicines and HealthCare Products Regulatory Agency (MHRA, UK).

The app was first piloted and made available in the UK, Netherlands and Croatia. The app was subsequently rolled out in Burkina Faso and Zambia with WHO support. The Med Safety app has been launched successfully in Armenia, Ethiopia, Cote d'Ivoire, Tanzania and Ghana.

Med Safety App offers a low-cost approach for National Medicines Regulatory Authorities to:

- collect, view and review ADR data submitted and directly linked to Vigiflow platform
- deliver safety messages, DHCPs, alerts, notices etc. to MAHs, HCPs and other stakeholders

Healthcare professionals and the general public please note that the App was launched on 4th September, 2020 and is available for download on Android and IOS on stores.

PHARMACOVIGILANCE: *A VIEW ON MEDICAL DEVICES*

The Nigerian National Pharmacovigilance Policy

The Nigerian National Pharmacovigilance Policy which was launched in 2013 addresses issues related to the systems and structures that are required for pre and post – authorization monitoring of safety and effectiveness of health products in Nigeria. The goal of the policy is to provide a strategic framework for the entrenchment of pharmacovigilance into the healthcare system in Nigeria to ensure overall safety in the use of medicines and other related products. Hence the Scope of Products for Pharmacovigilance Regulatory System in Nigeria is not limited to medicines but includes other related products such as vaccines/ biologics, medical devices, cosmetics, chemicals and herbals.

Medical Devices

The WHO defines a Medical Device as any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- investigation, replacement, modification, or support of the anatomy or of a physiological process,
- supporting or sustaining life,
- control of conception,
- disinfection of medical devices
- providing information by means of in vitro examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.[i]

Regulation of medical devices

In Nigeria, the National Agency for Food and Drug Administration and Control has the responsibility of ensuring that Medical Devices placed on the Nigerian market for use meet the requirements for Quality, Safety and Efficacy throughout the lifecycle of the product. The Act empowering NAFDAC for this role interprets a medical device as any instrument, apparatus or contrivance (including components, parts and accessories thereof) manufactured, sold or advertised for internal or external use in the diagnosis, treatment, mitigation or prevention of any disease, disorder, abnormal physical state or the symptom thereof, in man or in animal [ii].

To ensure proper regulation and safety monitoring of medical devices the Global Harmonization Task Force (GHTF) has prepared guidance document with set of rules which assist to allocate medical device to one of four classes using a set of classification rules which take account of the hazard presented by a particular device. The hazard presented by a particular medical device depends substantially on its intended use and the technology it utilises. Consequently, the classification rules stipulated in the guidance document take factors into account such as, whether the device:

• is life supporting or sustaining;

• is invasive and if so, to what extent and for how long;

• incorporates medicinal products, or human/animal tissues/cells;

• is an active medical device;

• delivers medicinal products, energy or radiation;

• could modify blood or other body fluids;

• is used in combination with another medical device[iii]

NAFDAC has adapted the international classification for regulation of medical devices in Nigeria as shown in table 1. Below

International Classification	Examples	Risk Level
A	Cholesterol, uric acid test system; Surgical Instrument; Bandage, Surgical camera; Electric operating table, Patient scale	Low
B	Pregnancy self-testing, Electric Hospital Bed, Surgical Lamp, Surgical Mask	Low – Moderate
C	Blood glucose self-testing, ECG, X-ray Unit, Syringe, Condom, Contact lens	Moderate - High
D	HIV Blood donor screening, Stent, Intraocular lens (IOL), Defibrillator, Pacemaker	High

It generally follows that regulatory control of medical devices by National Regulatory Authorities such as NAFDAC increases with increasing hazard or risk level of the medical device; more stringent regulations and monitoring apply to class D medical devices which are associated with the highest risk.

Post Marketing Authorization Safety Monitoring of Medical Devices

Two main approaches are employed in the Post approval monitoring of devices: Passive and Active surveillance or pharmacovigilance.

Passive surveillance involves submitting of spontaneous adverse events reports with use of devices to the NPC, by manufacturers or Marketing Authorisation Holders (MAHs), Healthcare professionals, and consumers. The NPC will then collate the information and determine if an intervention is needed.

Reports to be submitted may include issues of malfunctions, injuries, or fatalities associated with the use of Medical Devices. Such reporting is voluntary for the reporting health professionals or healthcare providers working in establishments other than the manufacturing or importing/distributing companies. It is a professional ethical obligation.

It is however mandatory for all Marketing Authorization Holders (MAHs) and manufacturers of medical devices to report to the NPC when they become aware of information that reasonably suggests that one of their marketed devices may have caused or contributed to a death or serious injury or has malfunctioned and the malfunction of the device or a similar device that they market would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.[iv] The MAHs and Manufacturers are to report such events occurring in Nigeria or anywhere in the world.

The NPC has deployed several channels for spontaneous reporting of adverse events to medicines and other pharmaceutical products such as the use of the yellow forms, the e-reporting platform and more recently, the med safety app which is publicly available on android and IOS stores.

In active surveillance or pharmacovigilance, active measures are taken to detect and report adverse effects/events. Such as active follow-up of patients and recording of all medical events. Follow-up may be done prospectively or retrospectively. There are 2 kinds of active post-approval surveillance for medical devices: conduct of prospective organized clinical studies and organization of active medical product registries capable of generating device safety and performance data[v]

NAFDAC, NPC is working towards a more active approach for safety monitoring of pharmaceutical products by way of Smart Safety Surveillance (SSS) initiative. SSS is a risk-based approach towards pharmacovigilance especially around the introduction of new medicines to treat priority diseases.

Benefits of Safety Monitoring of Medical devices

The primary aim of post marketing Safety Monitoring of medical devices is to improve the health and safety of patients or users and health care professionals by reducing the likelihood of reoccurrence of adverse events. Adverse event reporting is necessary to monitor medical device use and their performance in the real world and detect trends that may indicate emerging safety and performance issues. These activities will guide NAFDAC to take appropriate regulatory action to address the issues, thereby reducing the impact on the public.

A well-completed adverse drug reaction reporting form submitted could result in one or more of the following:

- Answer questions about the performance of certain devices
- Additional investigations into the use of the device in Nigeria.
- Educational initiatives to improve the safe use of the devices
- Changes in the labelling or Instructions for use of the devices to make them safer.
- Reclassification of rescheduling of medical devices
- Other regulatory interventions as the situation may warrant including corrective action for the device or withdrawal

All these translate to improvement on the quality of care offered to patients, hence, improved patient confidence in professional practice and consequently professional growth

Table 2. shows some Regulatory Decisions Taken as a Result of Pharmacovigilance

S/N	Drug	Reasons for action taken	Regulatory Decision taken	Year action was taken
1.	Tramadol	Irrational use and increased reports of ADRs	Reclassification of drug from POM to controlled drug	2012
2.	ISOTAB	Contamination of product	Targeted alert notice to HCP posted on Agency's website and NPC's newsletter	2012
3.	Gatifloxin	Risk of serious hyperglycaemia and hypoglycaemia	Ban of product and withdrawal of all brands from hypoglycaemia	2012
4.	Infusion fluid	Contaminated infusion	Mop up of affected batches, manufacturers GMP reevaluated, intervention in storage	2011
5.	Prevanar 13	AEFI reports of death from Prevenar 7 and insufficient evidence of efficacy and safety of prevenar 13 in Nigeria	Company directed to carry out phase IV study to ascertain safety and efficacy in the reduction of pneumococcal strains that are prevalent in Nigeria and the compatibility of vaccine with the vaccines used in routine immunization in Nigeria	2011

6.	Rosiglitazone	Risk of congestive heart failure	Recommendation for voluntary withdrawal by MAH	2011
7	Chlorzoxazone	Suspected hepatotoxicity	Dear Doctor letter to actively monitor the safety of the use of chlorzoxazone with regards to its potential to precipitate hepatotoxicity	2010
8	Formalin	Public misuse as an abortifacient	Reclassification from a general chemical to a restricted chemical	2010
9	Codeine containing cough mixtures	Public misuse	Public enlightenment	2010
10	Gentamicin 280mg/2ml	Increased risk of ototoxicity and nephrotoxicity and increased risk of endotoxin reactions	Recall/mop of gentamicin 280/2ml from circulation	2010
11	Teething mixture	Low benefit/risk ratio	Banned in Nigeria	2009
12	Abacavir (Ziagen®)	Serious hypersensitivity reaction	Review of core safety information by GSK to include HLAB*5701 gene testing	2008

Challenges

A review of individual case safety report (ICSRs) database at the Nigerian National Pharmacovigilance Centre (NPC) reveals that the Centre has not received any report of adverse events associated with the use Medical devices from 2004 to August 2020.

The U.S. Food and Drug Administration's Center for Devices and Radiological Health (CDRH) in a report titled "Ensuring the Safety of Marketed Medical Devices: lists the challenges of monitoring and assessing the safety of medical devices post marketing authorization. Some of these challenges apply to safety monitoring of medical devices in Nigeria and include

- Adverse events related to medical devices are widely under-reported. Even when a problem is detected, under-reporting makes it difficult to assess the true public health risk.

- Health-care providers generally don't document device use in patient records, making it difficult to identify the specific device involved when an adverse event occurs.
- Medical devices lack unique identifiers and manufacturers continually produce modified versions of their products.
- Devices are often used off-label, meaning they are used for indications and patient populations not included in the product's pre-market testing and approval.
- Medical devices are not just being used in hospitals and clinics but in patients' homes, which means more non-professionals are involved. This adds an element of uncertainty in diagnosing the cause of a problem and identifying possible solutions. [vi]

Pharmacovigilance of medical devices on the international scene

Regulatory Agencies around the world monitor the safety of medical devices to contribute to a better understanding of their possible adverse effects when they are used in real time outside of pre-marketing assessments.

In the United States, the Center for Devices & Radiological Health (CDRH) of the Food & Drug Administration (FDA) is specifically responsible for medical devices regulation. The FDA CDRH categorizes medical devices into one of three classes as Class I, II, or III based on their potential risks and the regulatory controls necessary to provide a reasonable assurance of safety and effectiveness. Class I devices generally pose the lowest risk to the patient and/or user and Class III devices pose the highest risk. Device classification by the US FDA also depends on the intended use of the device and its indications for use[vii].

A report on medical device reporting to the US FDA show that of about 4000 types of medical devices tracked by the institution, only 6 of those device types account for about 25% of the reports of adverse events (device injury) between 2008 to 2017. Table 3. Show device type most frequently reported on to the US FDA between 2008 to 2017

Device type	Class	Number of reports
Hip prosthesis	II	103,104
Insulin pump with senser	II	94,826
Spinal Stimulator	II/III	78,172
Surgical Mesh	II	60,795
Insulin pump implanted	II	60561
Defibrillator	II/III	59,457

Hip prosthesis is the device type with the highest number of reports (103,104) of adverse events/ injuries.[viii] The FDA highlights possible events that may occur after hip implant surgery, regardless of the type of hip system implanted, as follows:

- Hip dislocation, when the ball of the thighbone (femur) slips out of its socket in the hip bone (pelvis)
- Bone fracture
- Joint infection
- Local nerve damage with numbness or weakness
- Device loosening or breakage

- Difference in leg lengths
- Bone loss (osteolysis)
- Various types of local or systemic reactions to particles or ions generated from the use of the implant

Patients who have hip implants may observe symptoms that may occur three or more months after surgery that may indicate that their device is not functioning properly. These include:

- Pain in the groin, hip or leg
- Swelling at or near the hip joint
- A limp or change in walking ability
- Noise (popping, grinding, clicking or squeaking) from the hip joint[ix]

A retrospective study done in Colombia describing reports of adverse events or incidents related to medical devices between 2014 and 2017 showed that the devices that were most frequently reported as having events or adverse incidents were those belonging to the vascular access category, with 45.2% of cases, followed by surgical equipment, with 20.2%. The causes of the events or adverse incidents were most often failures of the mechanical components, at 50.6%, followed by manufacturing defects, at 28.7%.[x]

Conclusion

There is much work to be done in strengthening pharmacovigilance systems in Nigeria. The responsibility rests on all stakeholders: Government (e.g., Ministry of Health, Regulatory body, PHP), Marketing Authorization Holders, distributors, healthcare professionals, public health programs, patients and the general public. Some stakeholders have mandatory roles and others voluntary roles, both must be performed for results to be achieved.

NAFDAC implores healthcare providers to be relentless in the spontaneous reporting of Adverse events to pharmaceutical products that occur during their practice. This is a professional ethical obligation of the healthcare provider**.** The various reporting platforms deployed by NAFDAC: the ADR reporting forms, e-reporting platform and the med safety app can be used in sending individual case safety reports to the NPC.

Reports of adverse events to pharmaceutical products submitted to NAFDAC are treated with a high level of confidentiality and are used with a sole purpose of improving the healthcare system. It is important to note that the reporting of an adverse event does not make the MAH, healthcare professionals, patients or user liability for the event or its consequences.

NAFDAC PHARMACOVIGILANCE FOCAL PERSONS FOR STATES

In a bid to strengthen pharmacovigilance activities in all the 36 states of the Federation and the FCT, the Agency has assigned staff in each NAFDAC state office to be the focal persons for pharmacovigilance activities for the states. The focal persons have the responsibility of coordinating pharmacovigilance activities in the states, with roles such as:

- Disseminating and retrieval of ADR forms
- Pharmacovigilance advocacy
- Pharmacovigilance investigations

The Focal persons will liaise with the healthcare professionals, consumers and other stakeholders in the states and ensure that all

ADRs generated reach the National Pharmacovigilance Centre (NPC) promptly.

You may request the contact details of the focal persons for your state by sending us an email through pharmacovigilance@nafdac.gov.ng

GUIDE TO NIGERIA NPC ADVERSE DRUG REACTION (ADR) ELECTRONIC REPORTING (E-REPORTING) SYSTEM

The Nigeria NPC has deployed e-Reporting of ADRs. You may access this through the NAFDAC website: https://www.nafdac.gov.ng/

click on Pharmacovigilance & Post Market Surveillance link under **Services**. (bottom-left of the home page)

Select NAFDAC ADR e-Reporting Form under **useful resources** (right side of the page).

In filling the form:

- Please fill all Mandatory field(s) (*)
- Please indicate the "Weight" if available
- You can add as many reactions as possible by clicking on the "Add another reaction/symptom" box.
- Please indicate the "Outcome of reaction e.g. Recovered/Resolved
- Please indicate if the reaction(s) led to any of the following:
  - Caused Hospitalisation-initial or prolonged
  - Disabling/or permanent damage
  - Congenital anomaly/birth defect,
  - Life threatening
  - Death,
  - Require intervention to prevent permanent impairment or disability
  - Other medically important condition.
- It is important to report the following very important details even if they are not tagged as mandatory field (*);
  - Manufacturer of medicine Probably causing the reaction,
  - Strength (as stated on medicine packet)
  - Dosage (as taken)
  - Route (as administered or taken)
  - Place where medicine was obtained,
  - End date of medication or duration of use of the medicine,
  - Reason for taking the medicine
  - What else did you do (Action taken with medicine)
  - Has the medicine caused a similar reaction before?
- You can add as many medicines as possible by clicking on the "Add another medicine" box.
- DATES MEDICINES AND REACTIONS STARTED ARE VERY IMPORTANT.
- Please add any "Additional information" relevant to this case as stated in the form.
- Click on the "Next page" to proceed to the "Summary" page.
- View the summary of the report
- Submit by clicking the "Submit" box.
- After submitting, an acknowledgement is sent by WHO-UMC to the email address used for reporting the case.
- THANK YOU FOR REPORTING

Medical devices for pain, other conditions have caused more than 80,000 deaths since 2008 https://www.statnews.com/2018/11/25/medic

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