PHARMACOVIGILANCE/POST MARKETING SURVEILLANCE NEWSLETTER

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Regulation and Control of Medical Products in Response to COVID 19

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 focuses on Regulation and Control of Medical Products in Response to COVID 19 Pandemic.

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.

INTRODUCTION

The world is confronted with a serious pandemic, the outbreak of the novel Corona Virus Disease 2019, (COVID 19) caused by SARS-CoV-2. Currently, no effective antiviral treatments with acceptably proven efficacy for the disease or vaccine to prevent further spread of the virus have been confirmed. As a result, various Governments are continually devising ways of combating the disease and mitigating the socioeconomic and political effects of the COVID 19.

In Nigeria, the Nigerian Centre for Disease Control (NCDC) has published some basic precautionary measures to control person to person spread of the virus. Some of these measures involve the use of NAFDAC regulated products such as drugs, alcohol-based hand sanitizers, hand washing soaps, and use of face masks.

USE OF CHLOROQUINE PHOSPHATE (CQ) AND HYDROXYCHLOROQUINE (HCQ) TABLETS

Some clinical trials on Chloroquine and hydroxychloroquine are reported to show effectiveness of the products in COVID 19 treatment while others do not. For example, Multicentre clinical trials conducted in China has shown Chloroquine as one of the first drugs proposed as a treatment for COVID 19, and to have apparent efficacy and acceptable safety against COVID-19 associated pneumonia[i].

In another development, WHO on 17 June 2020, announced that hydroxychloroquine (HCQ) arm of the Solidarity Trial was stopped. Solidarity, is an international clinical trial coordinated by the WHO to help find an effective treatment for COVID-19. Data from Solidarity including the French Discovery trial data and the recently announced results from the UK's Recovery trial both show that hydroxychloroquine does not result in the reduction of mortality of hospitalised COVID-19 patients, when compared with standard of care[ii].

Clinical trial of chloroquine to evaluate its effectiveness in the treatment COVID 19 is ongoing in Nigeria. The trial has commenced in Lagos state, the Nigerian State most hit by the COVID 19. The results from this trial are necessary to determine whether or not Chloroquine can be adopted for the treatment of the COVID 19. Before now, Chloroquine has been discontinued for use in Nigeria for the treatment of P. falciparum Malaria due to concerns about species resistance.

NAFDAC, however, advises the public against the use of Chloroquine in non-clinical settings. Chloroquine can cause deafness, cardiac arrythmias and death, in addition to the common moderate to severe side effects including gastrointestinal upset, blurred vision, headache, and pruritis.

PRODUCT FALSIFICATION IN THE FACE OF COVID 19

In the wake of the pandemic, counterfeiters have turned their attention to focus on the products or commodities that are used to combat COVID-19. Hand sanitizers and chloroquine products are the most hit by the counterfeiters.

Falsified Chloroquine products

Several versions of falsified chloroquine products were found in circulation in the WHO region of Africa. Some of these have been shown to contain none of the stated active ingredients and are fraudulently manufactured to mimic genuine products.

The following public alerts on falsified chloroquine products have been placed on the NAFDAC website: www.nafdac.gov.ng/safety-alerts/

- Public Alert No. 005/2020 – Alert on Falsified Chloroquine Products Circulating in WHO Region of Africa
- Public Alert No. 004/2020 – Alert on Falsified Chloroquine Phosphate 250mg Tablets Circulating in Cameroon

Hand Sanitizers

Public Alert No. 003/2020 – Alert on Illegal Distribution and Sale of unregistered Hand Sanitizers was issued by NAFDAC to alert the members of the public on illegal distribution and sale of unregistered Hand Sanitizers. This was noted from the surveillance conducted by NAFDAC on prevalence of unregistered hand sanitizers in the Nigerian Market. Some unregistered Hand Sanitizers illegally distributed and sold under various names included

- Mighti Shield Instant Hand Sanitizer
- Assured Instant Hand Sanitizer
- One Step Hand Sanitizer
- Shield Germ Hand Sanitizer
- Lima Hand Sanitizer
- Senarita Hand Sanitizer
- AUS-B Hand Sanitizer
- Bakson Hand Sanitizer
- Peru Hand Sanitizer

The package labels of affected unregistered Hand Sanitizers have no NAFDAC Registration Numbers, no batch numbers, no manufacturing and expiry dates; no names and full location addresses of manufacturers.

The quality and safety of the unregistered Hand Sanitizers are not guaranteed because they are not evaluated by NAFDAC. The use of such products creates a false sense of security that the microorganisms on your hands have been neutralised, thereby putting the individual and others at increased risk of contracting infections.

The Agency has also received complaints from genuine manufacturers of some brands of hand sanitizers about falsification of their products that necessitated investigation and appropriate regulatory action.

NAFDAC advises the members of the public to only purchase hand sanitizers registered by NAFDAC and bearing all the required labelling information. The members of the public are implored purchase alcohol-based hand sanitizers from genuine verifiable sources

CLAIMS FOR COVID-19 REMEDIES

A press release articulating the Agency's position on claims for COVID 19 remedies was issued by NAFDAC and placed on the NAFDAC website on May 14, 2020,

In a bid to discover a cure for COVID 19, there were quite a number of unsubstantiated claims.

Complementary & Alternative Medicines Practitioners, Traditional healers, and the Academia are among the stake holders involved. It is pertinent to note, that these unsubstantiated claims are found in the conventional news media and the social media. The National Agency for Food and Drug Administration and Control (NAFDAC) as at the time of the press release had only received application from one company on a product the company is presenting to the Agency for consideration for the treatment of the symptoms of COVID-19, and not for the cure of COVID-19 as a disease. A claim of a cure must be subjected to clinical evaluation through well controlled, randomized clinical trials in line with an approved clinical trial protocol.

As an Agency saddled with the mandate of safeguarding the health of the citizenry, NAFDAC will continue to make sure that only medicinal product (including herbal remedies) that have proven safety data will be approved for use by the public.

Presently the Agency lists herbal medicines based on historical perspective on the use of the products after carrying out toxicological and microbiological evaluations to ensure that they are safe.

The listing status is valid for two years and is renewable. It does not validate the efficacy claims being made for the products. Hence, the labels must bear a disclaimer informing the consumer "The claims have not been evaluated by NAFDAC". This minimum requirement of 'proof of safety' is the Agency's way of encouraging production of herbal remedies from Nigeria's rich diversity of plants.

CONCERNS ON SELF-MEDICATION IN THE COVID 19 PANDEMIC

The onset of the COVID 19 and the increasing number of cases has advanced the course of self-medication as an increasing number of people opt for selfcare. Self-medication is defined as the use of drugs to treat self-diagnosed disorders or symptoms, or the intermittent or continued use of a prescribed drug for chronic or recurrent diseases or symptoms[iii]. It may include the use of herbs, the retention and re-use of prescription drugs or the direct purchase of prescription-only drugs without prescription from a qualified physician[iv].

Self-medication is not a new phenomenon. It plays important role in the management of minor illness. The use of Over-The-Counter (OTC) drugs including some analgesics, and antipyretics have benefit in treating minor ailments, although there are associated risky practices such as exceeding the recommended dose and not recognising adverse events.

The main concern with self-medication lies with the use of prescription drugs without expert advice from a qualified physician or the continued use of a prescribed drug beyond expert advice from a health professional. Prescription only medicines are usually associated with higher risks of occurrence of adverse events, hence the recommendation that they be used only on the advice of qualified health professionals.

Factors influencing self-medication

Self-Medication has been a challenge in the Nigerian Healthcare system and it is even more so now with the COVID 19 pandemic. A number of factors influence the surge in the practice of self-medication. These factors include: the fear

of hospitals as a potential harbour for transmission of the COVID 19; fear to be tagged a COVID 19 patient; publicising of certain medicines as effective/used in the treatment of COVID 19. A number of medicines including chloroquine, hydroxychloroquine and some antibiotics are the most implicated by this practice.

Risks associated with self-medication

A major risk associated with self-medication is the occurrence of Adverse Drug Reactions. The WHO defines an ADR as a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function[v]. Some ADRs are not consistent with applicable product information or characteristics of drugs unlike side effects which are related to the pharmacological properties of the drugs. While some adverse events are not serious, others are serious and may result in hospitalizations, disabilities and even death.

Self-medication is a major risk for occurrence of ADRs; insufficient knowledge about dosing, side effects, drug interactions and contraindications contribute to occurrence of ADRs. Members of the public may not be privy to risks associated with combining certain drug molecules or use of certain molecules in persons with underlying conditions. For instance, serious cardiac adverse events in patients with COVID-19 receiving Chloroquine or Hydroxychloroquine either alone or combined with Azithromycin or other QT prolonging medicines have been reported[vi].

Drug resistance is a well-documented phenomenon that is associated with Self-medication. Pathogen resistance has been a bane to healthcare delivery as antibiotics that were once very effective in treatment of certain conditions are no longer effective.

Generally, Potential risks of self-medication at individual level include the following:

- Incorrect self-diagnosis
- Failure to seek appropriate medical advice promptly
- Incorrect choice of therapy
- Failure to recognize special pharmacological risks
- Rare but severe adverse effects
- Failure to recognize or self-diagnosis contraindications, interactions, warnings and precautions
- Failure to recognize that the same active substance is already being taken under a different name
- Failure to report current self-medication to the prescribing physician (double medication/harmful interaction)
- Failure to recognize or report adverse drug reactions
- Incorrect route of administration
- Inadequate or excessive dosage
- Excessively prolonged use
- Risk of dependence and abuse
- Food and drug interaction
- Storage in incorrect conditions or beyond the recommended shelf life.[vii]

Guidance on self-medication

Members of the public are advised not to self-medicate with Chloroquine products. Healthcare professionals are implored to only use Chloroquine or Hydroxychloroquine in the context of clinical trials for the treatment of COVID-19. In addition, healthcare professionals are urged to:

- Ensure that patients receiving Chloroquine or Hydroxychloroquine for COVID-19 are adequately monitored to detect, document and report Adverse Drug Reactions (ADRs) associated with the use of the medicines.
- Ensure that pre-existing heart problems that can make the patients to be more prone to heart rhythm problems are properly documented during clinical trials.
- Report all concomitant medicines used in the management of COVID-19 during clinical trials including Azithromycin.
- Enlighten patients with COVID-19 on expected and unexpected ADRs that may be associated with Chloroquine or Hydroxychloroquine to enable the patients report their experiences with the use of the medicines.

Members of the public are also implored not to opt for self-medication but to seek proper medical attention

Healthcare providers and patients are encouraged to report adverse events associated with the use of these drugs to the nearest NAFDAC office, NAFDAC PRASCOR (20543 TOLLS FREE from all networks) or via pharmacovigilance@nafdac.gov.ng

[i] https://www.unboundmedicine.com/medline/citation/32074550/full_citation

[ii] https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

[iii] WHO (2000) Guidelines for the Regulatory Assessment of Medicinal Products for Use in Self-Medication.,Geneva. Available: http://apps.who.int/medicinedocs/pdf/s2218e/s2218e.pdf. Accessed August 17, 2019

[iv] http://www.emro.who.int/emhj-volume-17/issue-5/article8.html(22/07/2020)

[v] https://www.who.int/medicines/areas/quality_safety/safety_efficacy/trainingcourses/definitions.pdf

[vi] https://www.ahajournals.org/doi/10.1161/CIRCEP.120.008662

[vii] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4012703/