DrugLens

DrugLens Issue 1 March 2013

Message From The Chief Executive (Dr. Stephen K. Opuni)

I have the pleasure of introducing the first edition of DrugLens, a bi-annual publication by the National Pharmacovigilance Centre of the Food and Drugs Authority (FDA).

DrugLens will provide pertinent information regarding new and emerging drug safety issues in Ghana. This information will be used by health care professionals to assist in making the best decisions regarding the use of medicines and to promote the reporting of adverse drug reactions (ADRs).

ADR reports received from healthcare professionals will help the FDA in taking appropriate regulatory decisions regarding marketed products to ensure that patients derive the maximum benefit from pharmacotherapy.

DrugLens is also one of the FDA's commitment to building a world class regulatory authority by communicating timely and accurate safety information and other related activities to our stakeholders.

The first issue of this newsletter gives a summary of the ADR reports received over the past five years with emphasis on the 2012 reports, drug safety issues of current interest, pharmacovigilance awareness activities and safety monitoring activities by the National Pharmacovigilance Centre.

The FDA appreciates every healthcare professional who has completed our Adverse Reaction Reporting Form. Thank you for partnering with us to ensure the safety of patients.

Spontaneous Adverse Drug Reaction (ADR) Reporting for 2012

In 2012 the National Pharmacovigilance Centre through the spontaneous ADR reporting system received 325[1] suspected adverse drug reaction reports from healthcare professionals.

This is about 7 ADR reports per 1,000 000 population; which is significantly less than the WHO recommendation of 200 reports per 1,000,000 population[2].

The FDA together with the Expanded Programme on Immunization has set up a National system for reporting spontaneous Adverse Event Following Immunization. Sixteen reports were received from this system in 2012.

Figure 1 on the next page shows the breakdown of the number of reports received from different categories of healthcare professionals. 36.7% of these reports were received from Pharmacists.

[1].This report did not include those for vaccines; 16 AEFI reports were received through the spontaneous system in 2012

[2]. http://www.umc.org/DynPage.aspx?id=108476&mn1=7347&mn2=7252&mn3= 7322&mn4=7558

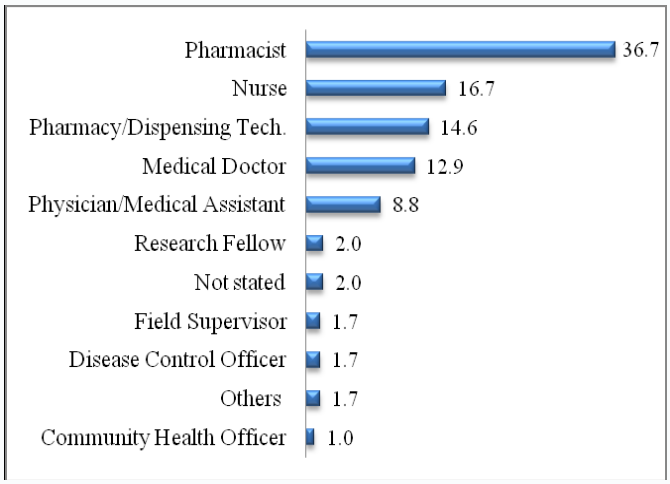


Figure 1: Percent Reporting by Healthcare Professionals

When the reports were classified into the System Organ Class (SOC) using the WHO-ART terminologies, skin and appendages disorders constituted the maximum number of reports received whereas urinary system disorder and reproductive system disorder, females constitute the least. The classification of reports as per the SOC classification is shown in Figure 2.

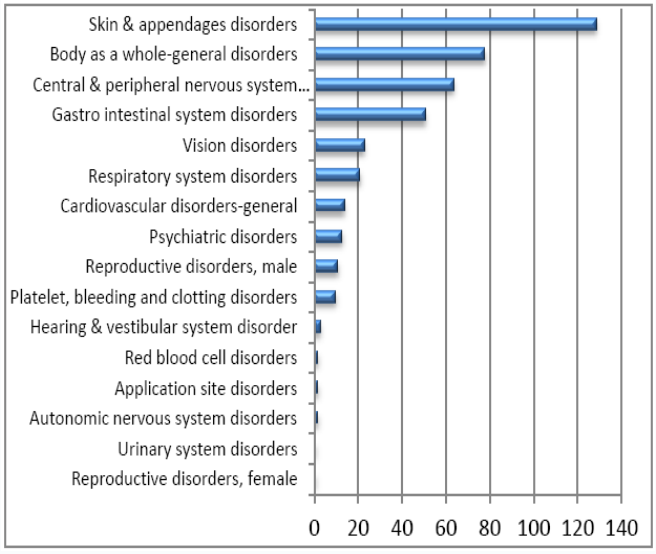


Figure 2: SOC Classification of the ADR

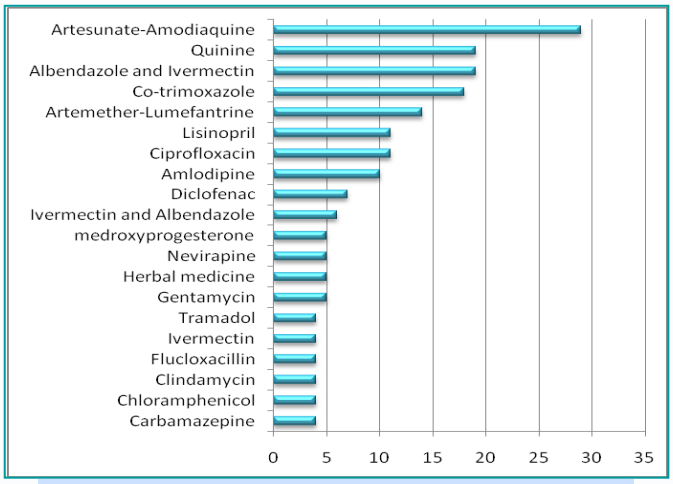


Figure 3: Top 20 drugs with most reported ADRs

Figure 3 displays the top 20 generic drugs for which spontaneous reports were received. Artesunate/Amodiaquine had the most number of spontaneous ADR reports.

The data revealed that females reported more ADRs (66%) to their healthcare professionals than males.

As shown in figure 4, 5% of the reactions reported to the FDA resulted in death of the patients. This is greater than the 0.32% reported in the ADR literature[3] and this may be due to the selective reporting of fatal ADRs by reporters in Ghana

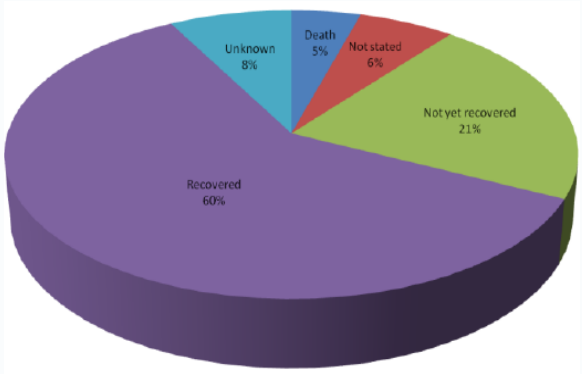


Figure 4: Outcome of the ADRs

Causality assessment of the reports by the Technical Advisory Committee on Safety using the WHO Causality Assessment Terminologies[4] revealed that 41% were Certain whereas 7% and 42% were probable and possible respectively. The rest were 3% unlikely, 4% unclassified and 3% unclassifiable.

Although the total number of reports received in 2012 were higher compared to the previous years (See fig. 5), this is about 14 reports per 1,000, 000 population in 2012 which is less than the WHO recommended annual reporting rate[5] of 200 reports per 1,000,000 population.

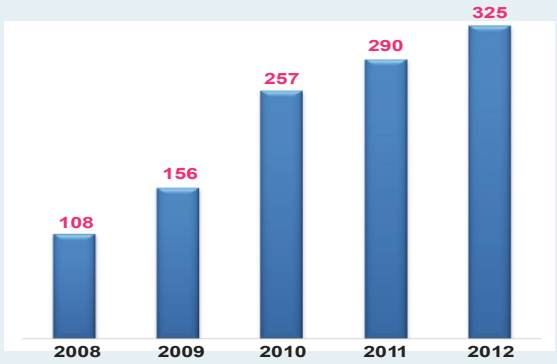


Figure 5: Annual Reporting for the past 5 years

The National Pharmacovigilance Centre would like to express its profound appreciation to healthcare professionals who took time out of their busy schedule to complete the ADR reporting form especially those from the Greater Accra and the Upper East Regions who contributed 27.7% and 21.5% of the reports respectively. Figure 6 showed the Regional reporting for 2012.

[3]Lazarou J., Pomeranz B.H., Corey P. N. (1996). Incidence of adverse drug reactions in hospitalized patients—a meta-analysis of prospective studies. *Journal of American Medical Association*, 279, 1200-5.

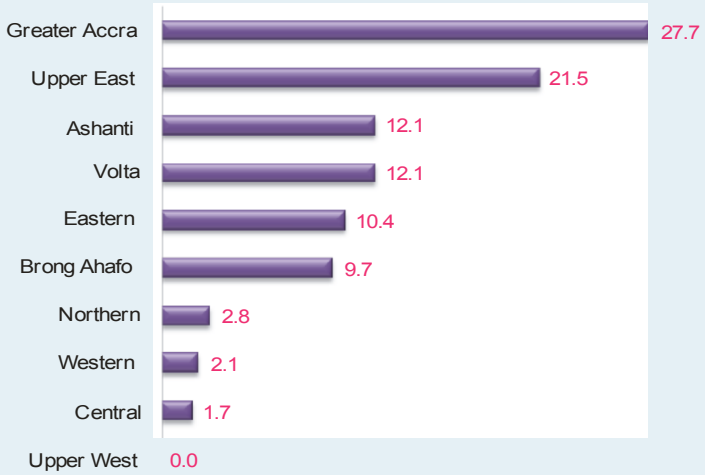


Figure 6: Percent ADR Reporting per Region

Safety Monitoring in the Public Health Act, 2012, Act 851

The Public Health Act, 2012, Section 125 makes safety monitoring of products granted marketing authorization and reporting of adverse events mandatory requirements for Local Representatives and Manufacturers.

Three subsections under section 125 summarize the responsibilities of the Manufacturer, Local Representatives and the FDA as follows:

1. A local representative for a regulated product shall be appointed by the relevant body.

2. The local representative:

a. Shall monitor the safety of the product granted marketing approval, and

[4]http://www.who-umc.org/Graphics/26649.pdf
[5]http://who- umc.org/DynPage.aspx?id=108476&mn1=7347&mn2=7252&mn3= 7322&mn4=7558

b. Shall report an adverse effect or event to the Authority during the period under which the product is registered.

The Authority shall continually monitor the safety of the products regulated under this ACT by analysis of the adverse effect or event reports and by any other means and take appropriate regulatory action when necessary.

The National Pharmacovigilance Centre, FDA, is taking steps to be able to execute its mandate. These strategic steps include the development of new guidelines which will guide all stakeholders as to new requirements, their specific roles and responsibilities to ensure compliance with the law.

The old guidelines for the reporting of adverse reactions have been improved to meet the new safety monitoring requirements. Additionally three new guidelines (listed below) have been developed to cover key areas in safety monitoring.

- Qualified Persons for Pharmacovigilance (QPPV)
- Pharmacovigilance Inspections
- AEFI Monitoring

The new guidelines when completed will be disseminated to Industry to enable them to meet the requirements in the Public Health Act, Act 851

Drug Safety Issues of Current Interest

Statins and the Risk of Diabetes Mellitus

Recent publications have linked HMG-CoA inhibitors (statins) to new-onset type 2 diabetes mellitus[6,7]. Individual statins may differ in the extent to which they increase the risk for new-onset type 2 diabetes mellitus.

In September 2012, the Medicines Adverse Reactions Committee (MARC) in New Zealand reviewed the relevant studies and concluded that there is a small, but statistically significant association, particularly in patients already at risk of type 2 diabetes mellitus[8].

The MARC concluded that the cardiovascular benefits of statin treatment clearly outweigh any risk of developing new-onset type 2 diabetes mellitus.

HMG-CoA reductase inhibitors registered in Ghana by the Food and Drugs Authority are Atorvastatin, Fluvastatin, Rosuvastatin and Simvastatin. Healthcare professionals in Ghana are therefore advised to closely monitor patients on statins and report any adverse drug reactions to the Food and Drugs Authority.

Concomitant Use of Simvastatin and Amlodipine or Diltiazem

The UK Medicines and Healthcare Products Regulatory Agency in August 2012 have recommended that for patients taking Amlodipine or Diltiazem the maximum dose of Simvastatin should not exceed 20mg per day.

[6] Sattar N, Preiss D, Murray HM et al. 2010. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. *Lancet* 375: 735-42.

[7] Culver AL, Ockene IS, Balasubramanian R, et al. 2012. Statin use and risk of diabetes mellitus in postmenopausal women in the Women's Health Initiative. *Archives of Internal Medicine* 172: 144-52.

[8] http://www.medsafe.govt.nz/profs/PUArticles/StatinsSept2012.htm

This is because research has shown that taking high doses of Simvastatin (more than 20mg per day) with Amlodipine or Diltiazem increases the risk of muscle injury[9].

Simvastatin is metabolised through the CYP3A4 pathway. Concomitant use of CYP3A4 inhibitors has the potential to increase exposure to simvastatin. Both amlodipine and diltiazem are substrates and inhibitors of CYP3A4 and therefore increase the plasma concentration (AUC0-24h) and maximum plasma concentration (Cmax) of simvastatin when they are co-administered. It is recommended that Simvastatin when given together with Amlodipine or Diltiazem should not exceed the maximum daily dose of 20mg.

Azithromycin and Cardiovascular Deaths

In May 2012, the New England Journal of Medicine published a study that compared the risks of cardiovascular death in patients treated with Azithromycin, Amoxicillin, Ciprofloxacin, Levofloxacin and no antibacterial drug[10].
The study reported a small increase in cardiovascular deaths and in the risk of death from any cause, in persons treated with a 5-day course of Azithromycin compared to persons treated with amoxicillin, ciprofloxacin, or no drug. The risks of cardiovascular death associated with Levofloxacin treatment were similar to those associated with azithromycin treatment. The US Food and Drugs Administration stated that it was reviewing the information but advised patients taking azithromycin NOT to stop taking their medicine without talking to their healthcare professional[11].

[9] Drug Safety Update August 2012 vol 6, issue 1: S1

[10] Wayne A. Ray, Katherine T. Murray, *et. al.*, (2012). Azithromycin and the Risk of Cardiovascular Death, *New England Journal Medicine*; 366:1881-90

[11] http://www.fda.gov/Drugs/DrugSafety/ucm304372.htm

Healthcare professionals were also advised to be aware of the potential for QT interval prolongation and heart arrhythmias when prescribing or administering antibacterial drugs.
Azithromycin belongs to a class of antibacterial drugs called macrolides, which have been associated with cardiovascular effects; specifically, prolongation of the QT interval. Prolongation of the QT interval can lead to torsades de pointes (TdP), an abnormal heart rhythm, which can be fatal. Azithromycin was the only macrolide examined in the published study; the study did not address other macrolide antibacterial drugs, such as clarithromycin and erythromycin, regarding the potential for cardiovascular deaths.

Safety Activities Monitoring

Cohort Event Monitoring of ACTs

In order to ensure the safety of anti-malarials, the Global Fund and the WHO have sponsored Cohort Event studies to ensure the safety and build public confidence on artemisinin-based combinations therapies (ACTs), artesunate and arthemether injection and oral and injectable quinine. The study sponsored by the Global Fund through the Affordable Medicines Facility for malaria (AMF-m) focused on only ACTs whereas the WHO sponsored study will consider all other antimalarials as listed above.

The AMF-m sponsored study started in January 2012 and is taking place in four Hospitals namely, Maamobi Polyclinic, Achimota Hospital, Effia-Nkwanta Hospital and Kumasi South Hospital. The WHO study began in October

2012 at Ho Municipal Hospital, Kintampo Municipal Hospital and War Memorial Hospital, Navrongo. Both studies are expected to recruit about 1250 patients from each site and will last for one year. Preliminary results from these studies will be provided in the next edition of the Drug Lens.

Active Adverse Event Following Immunization Monitoring of Vaccines

The National Pharmacovigilance Centre together with the Ghana Health Service (Expanded Programme on Immunization) have been involved in the active monitoring of the two new vaccines introduced into Ghana's immunization schedule (i.e. Rotavirus and Pneumococcal vaccines) through twenty sentinel sites throughout Ghana.

Participants during AEFI Monitoring Training Workshop in Tamale

The National Centre has also completed active monitoring of adverse events following immunization (AEFI) for Yellow Fever Phase II campaign in three regions, namely, Brong Ahafo, Ahanti and the Volta Regions. AEFI monitoring for the MenAfriVac vaccination campaign is also completed in the three northern regions.

Please, look out for the results from these activities in the next edition of the DrugsLens.

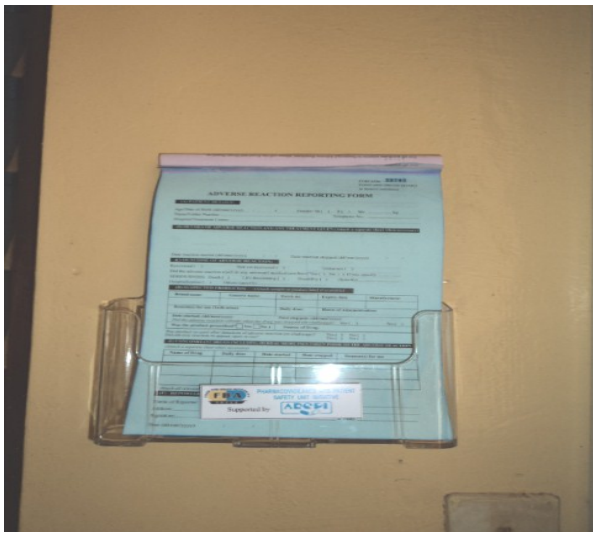
Drug Safety News

FDA Collaborates with AREPI

The National Centre in collaboration with the Association of Representatives of Ethical Pharmaceutical Industries (AREPI) has began a pilot programme to improve ADR reporting in Ghana using ADR Reporting Forms plastic holders. This is aimed at making the reporting forms readily accessible at healthcare institutions.

To this AREPI donated 100 plastic holders to be mounted at vantage points in wards in selected institutions.

The beneficiary institutions are encouraged to make maximum use of the easy accessibility of the reporting forms in the facilities to increase ADR reporting.



Sample of the ADR Form Holder at Legon Hospital

Pharmacovigilance Awareness Programmes

The Centre routinely organizes pharmacovigilance awareness programmes for healthcare professionals in government, quassi and private healthcare facilities. Some of the institutions, sensitized in 2012 include Ridge Hospital, Castle Clinic, Old Ningo Health Centre, TUC Base Clinic, Ridge OPD, Ashiaman Polyclinic, Makola Government Clinic, Central Aflao Hospital and St. Mary Theresa Hospital for a total of 245 healthcare professionals.

The Centre also sensitizes healthcare professional groups on Pharmacovigilance and the need for their contribution to the Safety Monitoring System in Ghana. Some of the professional groups sensitized include the Pharmaceutical Society of Ghana during the 2012 Annual General Meeting and members of the Association of Private Medical and Dental Practitioners, also at their 2012 AGM.

We hope to improve on this performance in 2013 and appeal to Heads of Healthcare Institutions to cooperate with the Centre in its effort to ensure patient safety.

Pharmacovigilance awareness program at the Sweden Ghana Medical Centre Ltd.

Technical Advisory Committee for Safety

The year 2012 was the busiest for the members of the Technical Advisory Committee for Safety. This is because apart from the quarterly meetings of the Committee, there were three different National Expert Committees set up to review reports from the active safety monitoring programmes during the year.

Most of the members of the Committee were also members of the National Expert Committees (NEC) for MenAfriVac, Yellow Fever and the two New Vaccines (Rotavirus and Pneumococcal Vaccine) incorporated into the Expanded Programme on Immunization Schedule.

Section of members at the 28th TAC Meeting

We are very grateful to all members and the co-opted members who helped in the evaluation of over 5000 reports received from the spontaneous and the active monitoring programmes last year.

The National Centre in the coming years will continue to rely on the expertise of the members of the Committee in ensuring medicine safety in Ghana.

Suggestions

Your comments are important to us. Help us
improve on what we are doing by reaching us on the contacts below:
Tel: **0244 310 297**
E-mail:drug.safety@fdaghana.gov.gh

Reporting Adverse Reactions
You can report adverse drug reactions by calling the National Pharmacovigilance Centre on:
0244 310 297

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