ANNUAL REPORT

NATIONAL DRUG AUTHORITY

Annual Pharmacovigilance Report
July 2015 – June 2016

Safe Drugs Save Lives

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PREFACE

For all medicines there is a trade-off between the benefits and the potential for harm. To minimize the harm, it is necessary that medicines of good quality, safety and efficacy are used rationally, and that the expectations and concerns of the patient are taken into account when therapeutic decisions are made.

Studies show that almost half (49.5%) of all hospitalized patients in Uganda are prone to experiencing an ADR[1]. Despite this, under-reporting of ADRs frustrates efforts in identifying, evaluating and preventing several unusual, serious, hazardous and novel ADRs, and thus under estimating their burden in populations[2]. This may consequently lead to increased medicine-induced morbidity and mortality. Additionally, ADRs impart economic constraints on public health systems[3].

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> There is a realization that Pharmacovigilance is more than the monitoring, detection and assessment of ADRs occurring under clearly defined conditions and within a specific dose range, rather, it is closely linked to the patterns of drug use within society.

The scope of Pharmacovigilance activities continues to broaden as the array of medicinal products grows. There is a realization that Pharmacovigilance is more than the monitoring, detection and assessment of ADRs occurring under clearly defined conditions and within a specific dose range, rather, it is closely linked to the patterns of drug use within society.

The National Pharmacovigilance Centre (NPC), under the National Drug Authority, has strived to match the widening scope of medicine safety by engaging in a wide range of activities .This report highlights the major Pharmacovigilance activities that took place between July 2015 and June 2016, including the major advance in the field of reporting, which is the electronic reporting of ADRs.

Donna Kusemererwa

Secretary to the Authority

CONTENTS

ACKNOWLEDGEMENT

This report presents the tireless and collective effort of many stakeholders that are committed to promoting medicine safety by monitoring and reporting adverse drug events and other drug related problem.

The National Pharmacovigilance Center (NPC) wishes to thank all the health workers in the country that have continuously taken time to report adverse events.

We appreciate the effort of the Pharmacovigilance coordinators in the country who have been at the fore front in co-ordinatating activities in regional referral hospitals and their catchment facilities. We appreciate Akello Harriet, Anguma Daniel, Martha Ajulong, Leo Atwine, Rodney Tabaruka, John Kizito, Dr.Patrick Musinguzi, Ignatious Akankwasa, Dr.John Twinomuhangi, Kyalimpa Leonard, Ouma David and Atim Goretti.

Last but not least, I applaud the national Pharmacovigilance centre staff for working hard to ensure that Pharmacovigilance keeps afloat.

Thank you Victoria Nambasa, Huldah Nassali, Julius Mayengo, Evans Tusubira. Wendy Gilda Nyamusana (intern pharmacist) we appreciate your contribution

Helen Ndagije

Head National Pharmacovigilance Centre

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The National Pharmacovigilance Center (NPC) wishes to thank all the health workers in the country that have continuously taken time to report adverse events.

ABBREVIATIONS

ADR	Adverse Drug Reaction
AEFI	Adverse Events Following Immunization
AIDS	Acquired Immune Deficiency Syndrome
AMR	Antimicrobial Resistance
EAC	East African Community
EPI	Expanded Programme on Immunisation
ICH	International Committee on harmonization
ICSR	Individual Case Study Reports
IPT	Intermittent Prophylactic Treatment
MAAIF	Ministry of Agriculture, Animal Industry and Fisheries
MSH	Management Sciences for Health
NaLIRRI	National Livestock Resources Research Institute
NDA	National Drug Authority
NMS	National Medical Stores
NPC	National Pharmacovigilance Centre
NTLP	National Tuberculosis and Leprosy Program
PMS	Post Marketing Surveillance
PNFP	Private Not for Profit organisations
RPC	Regional Pharmacovigilance Centre
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
SOC	System-Organ Class
TB	Tuberculosis
TOT	Training of Trainers
UMC	Uppsala Monitoring Centre
VICHOF	International Committee on Harmonization for the Registration of Veterinary Medicinal Products Outreach Forum
WHO	World Health Organization
WHO-ART	WHO Adverse Reaction Terminology

EXECUTIVE SUMMARY

> To minimize the harm, it is necessary that medicines of good quality, safety and efficacy are used rationally, and the expectations and concerns of the patient are taken into account when therapeutic decisions are made.

For all medicines, there is a trade-off between the benefits and the potential for harm. To minimize the harm, it is necessary that medicines of good quality, safety and efficacy are used rationally, and the expectations and concerns of the patient are taken into account when therapeutic decisions are made. To achieve this is to serve public health, and to foster a sense of trust in patients in the medicines they use that would extend to confidence in health service in general.

During the index period, a total of 174 reports were received from the different regional Pharmacovigilance centre with antiretrovirals being reported most. Urinary tract disorders, masculo-skeletal disorders and skin reactions, in that order were among the most reported reactions.

Introduction of e-reporting tool for ADRs, continuous awareness campaigns on medicine safety and capacity building of stakeholders in ADR monitoring are the key successes of any Pharmacovigilance program. There has been different trainings of Health Care Practitioners (HCP) and intern pharmacists during the index period. Different national and international collaborations have also been enhanced.

1 INTRODUCTION

The National Pharmacovigilance Centre was established in late 2004 having been delegated to NDA by ministry of health to carry out safety monitoring of drugs. The centre draws its mandate from the National Drug Policy and Authority (Pharmacovigilance) Regulations, 2014.

The centre attained full membership to the WHO Collaborating Centre on International Drug Monitoring (UMC) in June 2007 and is now the 83rd member country.

1.2 Objectives of the centre are;

- To coordinate, collect, analyze and evaluate adverse drug reaction reports on medicines in the country.
- Promote exchange of drug information with Drug Information Centres within and outside the country.

1.3 Pharmacovigilance advisory committee

The national Pharmacovigilance centre is resourced with an expert advisory committee that is responsible for guiding development, implementation and evaluation of policies for the following:

- Strengthening the monitoring of adverse events and reactions to medicines.
- Strengthening the regulation of drug-related clinical trials and veterinary field trials.

Promotion of public awareness and sensitisation of users of veterinary medical products in relation to their correct handling and use

2 REPORT ON ACHIEVEMENTS IN THE FINANCIAL YEAR 2015/2016

The main strategic objective of the centre for the reporting period was to ensure that essential, safe, efficacious and cost-effective drugs and other healthcare products are made available to the entire population to provide satisfactory healthcare. This was to be achieved through strengthening spontaneous reporting of adverse events and active monitoring of medicines of public interest.

2.1 Adverse Drug Reaction Collecting Mechanism

2 1.1 Introducing a web service to report adverse reactions

Since inception of the National Pharmacovigilance Centre, reports of suspected adverse drug reactions and many other drug related problems have been received mainly from health care professional using the national reporting form. One of the challenges faced by the use of the reporting form is the delay in relaying information from the reporter to the national centre. The delay could mostly hamper timely assessment and feedback on the suspected adverse event especially if it is of serious a nature.

The National Pharmacovigilance Centre introduced online reporting of suspected Adverse Drug Reactions (ADRs). Reports from health-care professionals and patients (in the future) can be entered via the e-Reporting tool and all reports go to the National Centre in VigiFlow.

2.1.2 Who can use the tool?

All Health care providers (clinicians, dentists, pharmacists, nurses etc), and consumers (in the future) .

2.1.3 How to report?

To report a suspected ADR online, please visit: *https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=UG*

2.2 Status of Individual Case Reports (ICRS): Reporting, Collation And Analysis

A total of 174 ADR reports were received at the National Pharmacovigilance Center (NPC) in the period of July 2015 to June 2016. These reports were derived entirely from spontaneous (passive) reporting system. All the reports received were reviewed for validity and causality before finally submitting to the WHO global database. Although there is no clear trend in the monthly ADR cases reported this year as illustrated in the figure 1 below, there was an improvement in timeliness of reporting by healthcare workers.

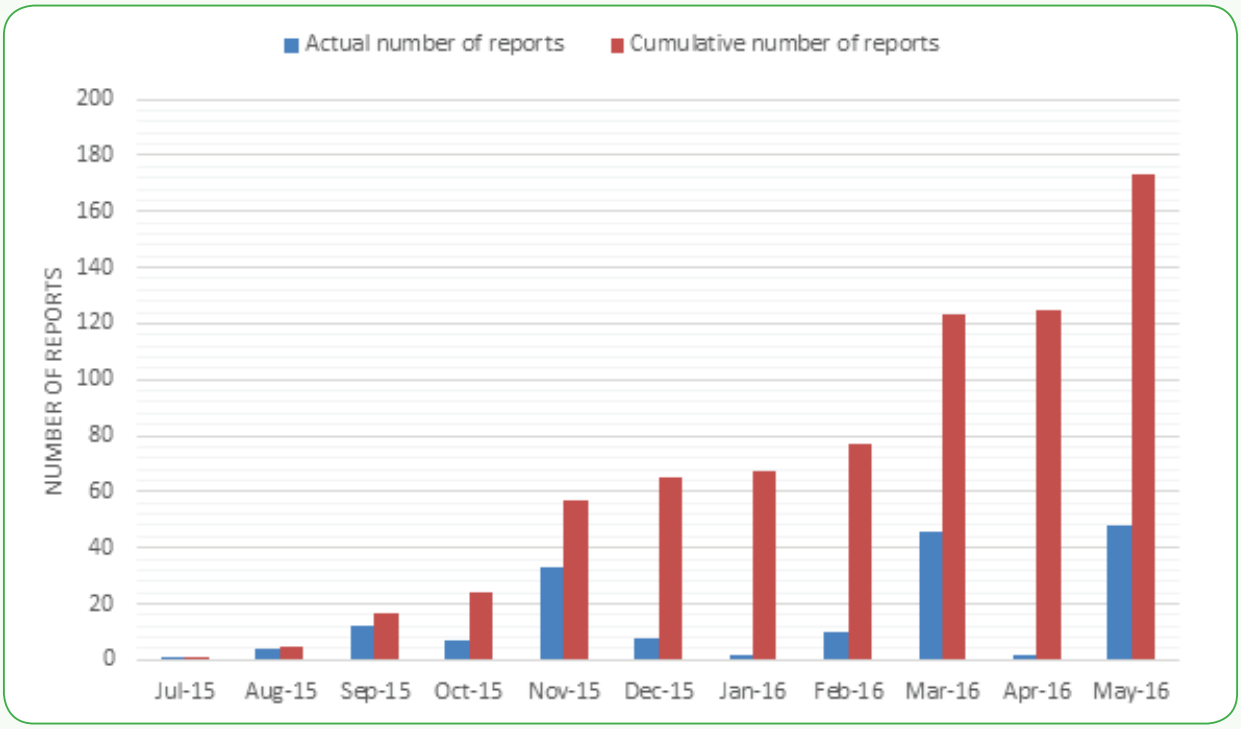

Figure 1: ADR reports received from districts in each month

ADR reports received came from only 16 out of 112 districts (Figure 2) with Masaka leading in the reporting. All the reports from for example Wakiso, Masaka, Kabalore and Mubende came from facilities and departments like the HIV section that are heavily supported by development partners.

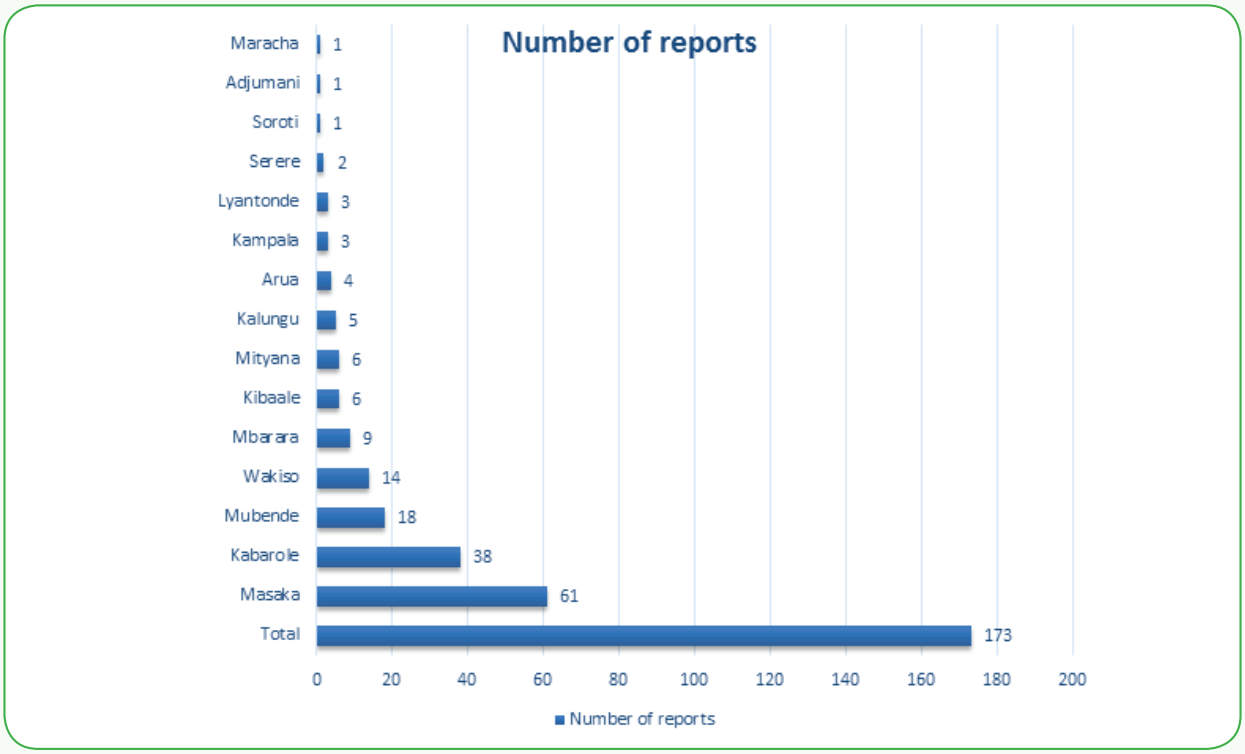

Figure 2: Breakdown of the number of reports received per district

Facility type: Private Not For Profit (PNFP) institutions submitted the highest number of reports followed by Hospitals, as shown in figure 3. Only one case report was received from a private pharmacy /drug outlet.

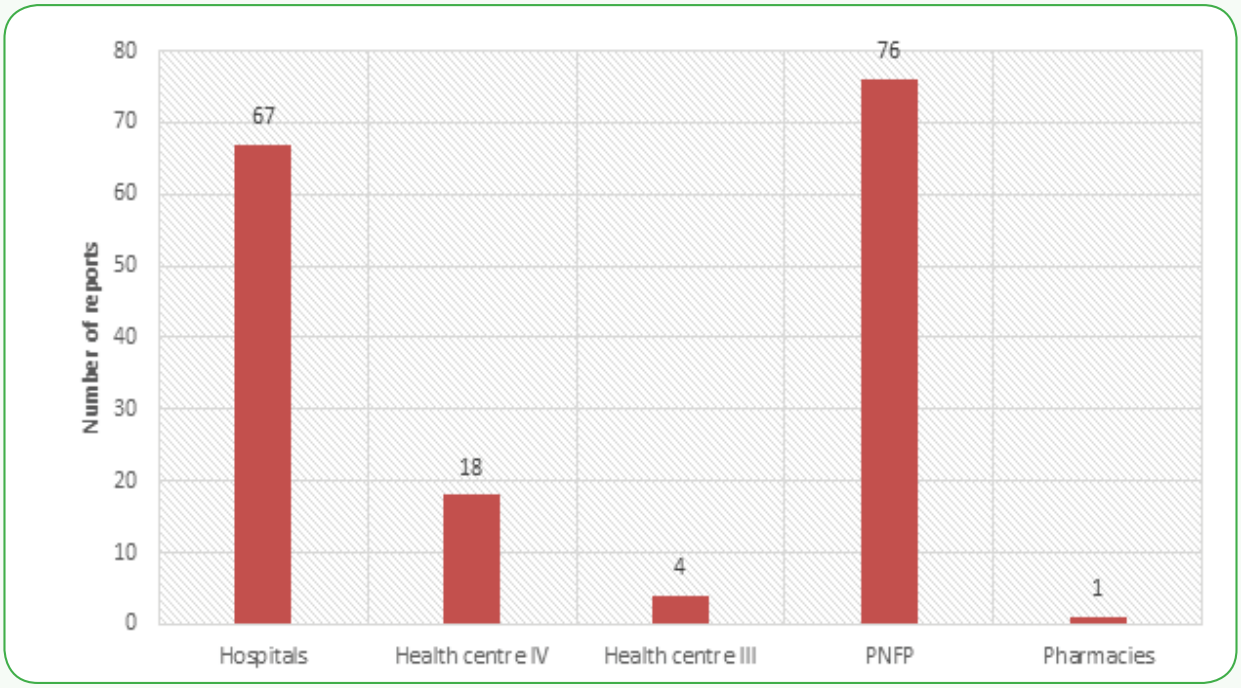

Figure 3: Reports received from different levels of health care facilities

Among health facilities, Uganda Cares (Masaka Hospital) submitted the highest number of reports followed by Fortportal regional hospital. The performance of various health facilities is shown in figure 4 below.

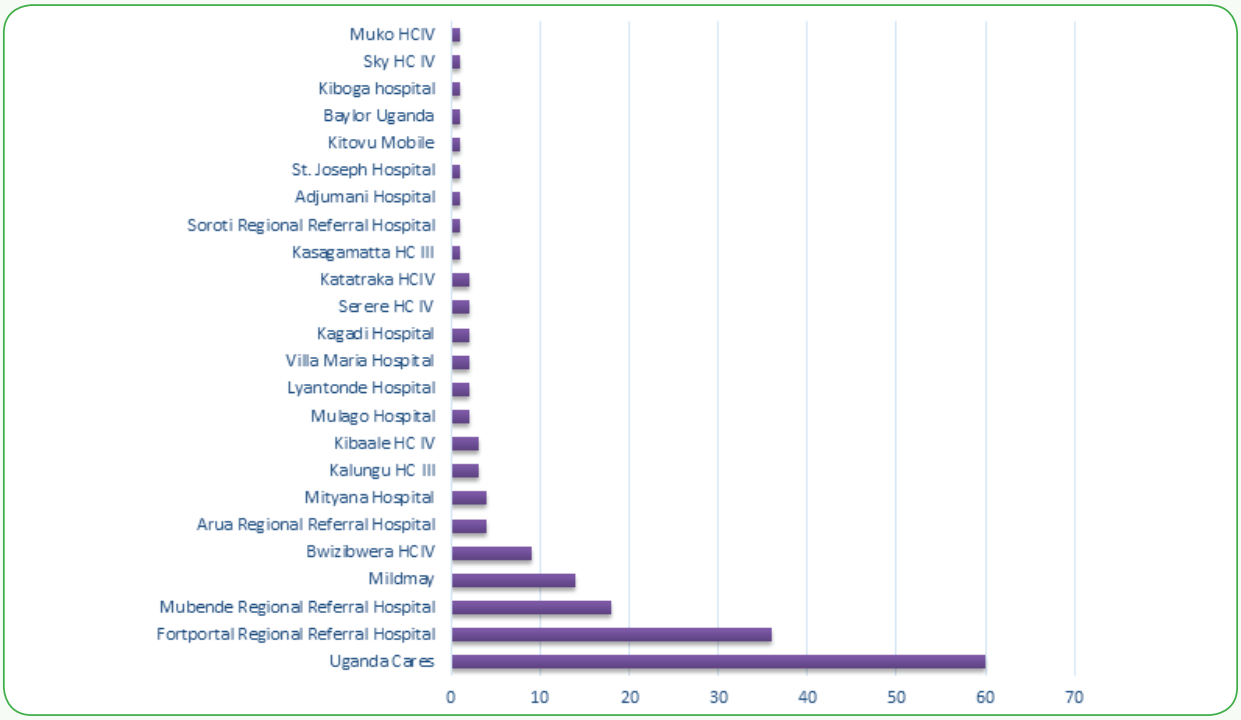

Figure 4: Number of reports received per health care facility

2.3 Suspected Adverse Drug Reaction Profile

The reported ADRs included a large spectrum of clinical manifestations, which are summarized based on WHO Adverse Reaction Terminology (WHO-ART) and System-Organ Class (SOC). Suspected adverse drug reactions of Urinary tract disorders (kidney dysfunctions (oedema, raised serum creatinine)) were reported most (43.7%) followed by skin reactions (36.8%). Musculoskeletal disorders (conditions related to bones and muscles) presenting as osteomalacia /bone demineralization were also among the most reported (Figure 5).

The observed trend could be explained by the current massive use of Tenofovir as the preferred regimen for treatment of HIV. The reporting rate is also correlated with the most reported drug which was Tenofovir as shown in Figure 6 below.

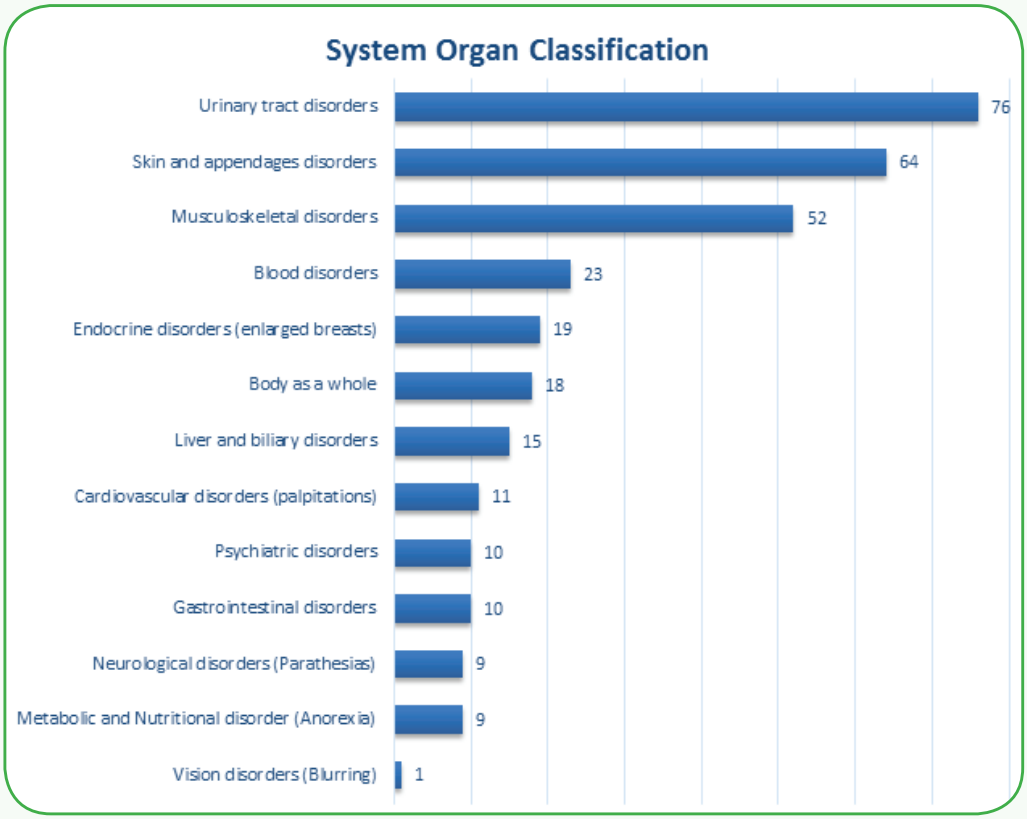

Figure 5: frequency of suspected ADR based on SOC

2.4 Common Reported Drugs

Antiretroviral drugs had the highest number of reports (80.35%) as shown below

Drug class	Number of ADR reports
Antibacterials	14
Antimycobacterials	6
Antivirals	1
Antimalarials	4
Antiretrovirals	139
Anticancers	1
Anasthetics	3
Contraceptives	1
Anticonvulsants	1
Antihypertensives	1
Vaccines	2

Tenofovir, Efavirenz and zidovudine were the antiretroviral drugs that had the highest number of ADRs reported. Tenofovir was reported to be associated with renal abnormalities and masculo-skeletal disorders (detailed report provided as annex 1), while Zidovudine was majorly associated with aneamia with a few with on lipodystrophy. Efavirez was mainly associated with gynaecomastia and psychosis. Below is the breakdown of the top ten reported drugs during the index period;

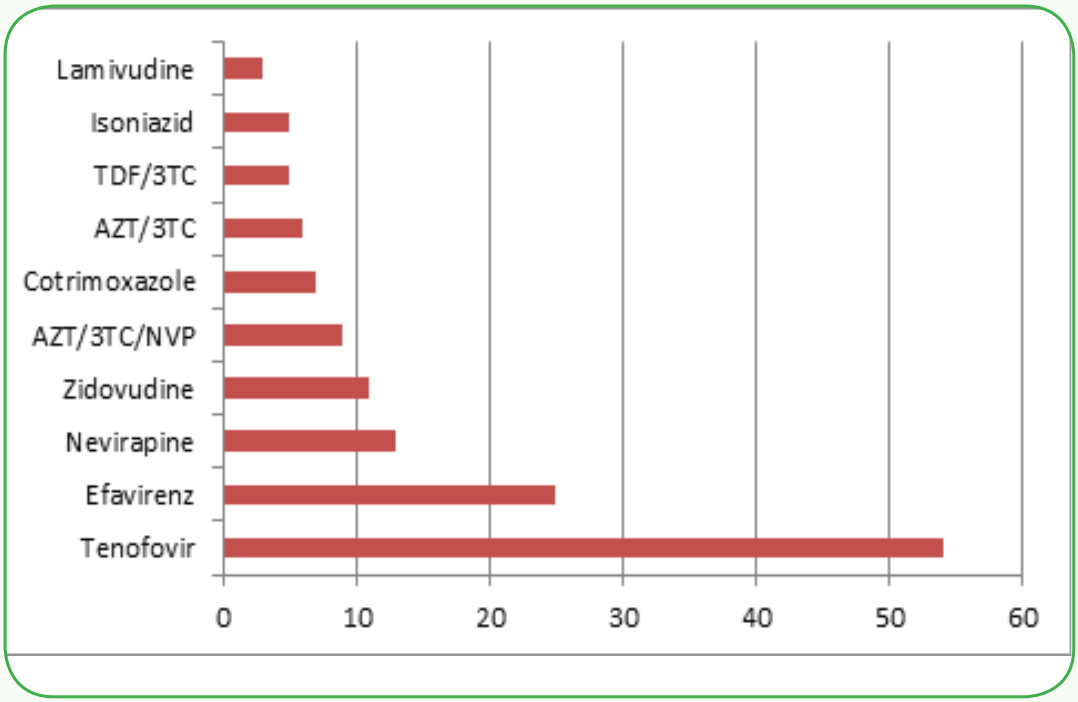

Figure 5: Drugs and the number of suspected ADRs

Antiretroviral drugs were not the only reported drugs during this index period. The table below lists the common adverse drug reactions associated with each individual drug as reported;

Drug(s)	ADRs
Artemether- Lumefantrine	Red eyes, fever, severe headache
Doxycycline	Headache, Anaphylaxis
Cotrimoxazole	Severe thrombocytopenia with low Hb, hyperpigmentation of the skin, skin rash and itching, general body weakness
AZT/3TC	Anemia, hyperpigmentation of skin, palpitations, lower limb swelling, hepatotoxicity
Isoniazid	Dry scaly skin rash, swollen limbs, anorexia, fever, skin itching, abdominal pain, general body weakness
Amoxicillin	Skin rash and itching
Etonogestrel	Skin rash
Kanamycin	Hearing impairment
Captopril	Blurred vision, diarrhea
Bleomycin/ Vincristine	Swollen face up to the neck, upper body rash and itching
AZT/3TC/NVP	Palpitations, oedema, severe anemia, enlarged liver, generalised non-itchy rash,
TDF/3TC	Parathesias, arthralgia, facial puffiness
Zidovudine	Anemia, Redness of eyes, swollen upper limbs
Nevirapine	Generalised skin rash, jaundice
Lamivudine	Generalised skin rash
Tenofovir	Increased serum creatinine, bone demineralization, osteomalacia, reduced bone density, odema, facial puffiness, fanconi syndrome, joint pain, limping gait
Bupivacaine	Increasing sensory blockade, failed spinal anaesthesia
Acyclovir	Generalised erythema of skin with marked itching
Benzathine Penicillin	Anaphylaxis
ABC/3TC	Nausea and vomiting, collapse
Artesunate	Urticaria, oedema
Efavirenz	Engorged breasts, skin rash, night mares, insomnia, chest pain
TDF/FTC/EFV	Joint pain, general body weakness, limping gait
TDF/FTC	Hepatotoxicity, marked jaundice
Carbamazepine	Generalised scaly rash
Rifampicin	Yellowish eyes
TDF/3TC/EFV	Generalised itchy skin rash
sulfadoxine/ pyrimethamine	Red papules plus swelling of the body especially breasts and mouth
AZT/3TC/EFV	Prolonged vomiting and dizziness,
Dpt-Hib-HepB	Abscess at injection site
Oral Polio vaccine	Skin pustules, some of which burst to form superficial wounds
Atazanavir/r	Lipodystophy, severe hyperbilirubinemia
lopinavir/r	Diarrhoea

2.5 Reports submitted on quality problems

Several reports of products with substandard quality were reported through the Pharmacovigilance system. Drugs reported include: insulin, Ceftriaxone, hydralazine, calcium lactate, bupivacaine. Other products reported include: Injections and infusion sets and health consumables. Investigation of these complaints is ongoing.

3 REGIONAL HARMACOVIGILANCE CENTRE (RPC) ACTIVITIES

Following the establishment of the national Pharmacovigilance centre, there was country wide sensitization of health workers and distribution of adverse drug reaction forms. This followed establishment of the regional Pharmacovigilance centres hosted by regional referral hospitals in the country. To date there are 13 regional centres overseen by coordinators. Coordinators in the regions are tasked to do the following

1. Develop and implement a plan for strengthening PV within the hospitals and catchment facilities, and coordinate all on-going Pharmacovigilance activities in the hospital.

2. Support health workers/facilities by availing reporting tools, organizing trainings/capacity building, retrieving filled ADR reports from the catchment facilities. The coordinator will ensure catchment facilities have functioning Pharmacovigilance systems

The national Pharmacovigilance centre has supported the regional centres by providing regular logistical support, mentorship and supervision in order to build their capacity to carry out Pharmacovigilance activities.

Ten (10) centers were visited during this period. Trainings of new staff, delivery of reporting material, and retrieval of safety reports were done.

4 STRENGTHENING ADR REPORTING FOR DOCTORS AND STUDENTS

Development of Pharmacovigilance skills during the formative years of medical training is key to instill a reporting culture. To this end, NDA carried out trainings and awareness sessions in 9 (nine) institutions in South Western Uganda (Mbarara University, Kisiizi Nursing School and Kabale Nursing School) and Northern Uganda (Gulu University, Gulu School of Clinical Officers, Lacor School of Nursing, and Gulu Institute of Health Sciences).

In Mbarara, a Pharmacovigilance public awareness day was also carried out by the students to create awareness among the public on the value of reporting drug related reactions.

5 COLLABORATIONS

5.1 Regional and International

Collaboration was done with Baylor to support Pharmacovigilance in the Eastern region of Uganda. NDA provided the tools, and facilitated training in some areas like Kachumbala and Bukedea.

Newsletters and publications containing safety issues on various drugs from world health organization, Uppsala Monitoring Centre (UMC) and Egyptian Pharmacovigilance centre were received. Some of the safety issues were published in the Pharmacovigilance bulletin.

The centre participated in harmonization activities at the East African Community (EAC). Participation was done in the development of Pharmacovigilance indicators.

The centre also participated in the 38th Annual meeting of Representatives of the National Pharmacovigilance Centre participating in the WHO Programme for International Drug Monitoring, held on 3rd to 6th November 2015 in New Dheli, India. During the meeting, the national Pharmacovigilance centre presented a paper on medication errors.

5.2 Collaborations to Promote Pharmacovigilance In Public Health Programs

5.2.1 National Tuberculosis and Leprosy Program (NTLP)

The centre has worked with NTLP to establish a Pharmacovigilance component within the TB programme. A framework to ensure clinical, administrative and political support throughout the process has been developed. A team consisting of key representatives from the NTLP, NDA and MSH/ Systems for Improved Access to Pharmaceuticals and Services (SIAPS) was constituted to coordinate the implementation at the national level.

Mildmay Uganda is partnering with National Drug Authority to monitor adverse drug reactions. Targeted spontaneous reporting of Isoniazid used for Intermittent Preventive Therapy and monitoring of adverse drug reactions experienced during use of anti TB drugs at Mildmay sentinel sites has been implemented. Mildmay is supporting NDA to train and mentor its support centres in various districts to monitor Isoniazid use in IPT as it is being rolled out in the country.

5.2.2 Expanded Program on Immunization (EPI)

Vaccine surveillance needs to be more efficient and robust in order to pick any safety events before they negatively influence the vaccination activities. This has gained increased importance because many vaccines are being manufactured in new methods and there are some newer antigens. One of the steps for strengthening vaccine surveillance in the country is to merge tools utilized by the UNEPI and by the NPC for documenting AEFIs. The NPC has coordinated merging of the tools (forms and guidelines) and is in the final stages of merging the form.

The AEFI and ADR reporting forms were merged into one form and pretested to measure its applicability.

5.2.3 The role of Pharmacovigilance to drug policy

The National Drug authority together with the AIDS control program assessed a number of suspected adverse drug reactions possibly related to Efavirenz. Reinforced by the data from one of the genetic studies in Uganda , the team recommended a change of Efavirenz dose from 600 to 400 mg. This change is to be included in the ART guidelines for Uganda after a thorough review process.

6 COMMUNICATION & FEEDBACK

The National Pharmacovigilance centre developed three Pharmacovigilance bulletins in which medicine safety issues were shared with the health professionals. The bulletin is a channel for sharing information relating to drug safety issues country wide and internationally. Through these bulletins, the NPC publishes information from the ADR reports that health professionals send as a way of giving feedback.

Publication in peer reviewed journals

Helen Ndagije, Victoria Nambasa, Elizabeth Namagala, Huldah Nassali, Dan Kajungu, Gordon Sematiko, Sten Olsson, Shanthi Pal. (2015) Targeted Spontaneous Reporting of Suspected Renal Toxicity in Patients Undergoing Highly Active Anti-Retroviral Therapy in Two Public Health Facilities in Uganda. Drug safety 03/2015

7 VETERINARY PHARMACOVIGILANCE

National Drug Authority has been accepted as a member of the International Committee on Harmonization for the Registration of Veterinary Medicinal Products Outreach Forum (VICH OF). This aims to build veterinary regulatory systems by accessing and using internationally accepted guidelines and documents. In Africa it is only Uganda, Tanzania, Morocco and South Africa who are members.

NDA has joined the global campaign on antimicrobial resistance originating from the irrational use of antibiotics in food producing animals like poultry, cattle, pigs and goats. Contribution was made to the global database by submitting the quantities of antibiotics imported in the country in 2010 and 2011. NDA is participating in a World Bank study entitled "The Economic Cost of Antimicrobial Resistance" targeting antibiotic use in animals as a driver for AMR.

NDA participated in the national celebrations of World Veterinary Day on the 30th April in Makerere University. Newsletter volume 1 issue 2 that focused on veterinary issues was shared with stakeholders. Complaints were picked from this meeting on farmers resorting to using ivermectin for control of ticks which brings food safety issues because of its long withdrawal period from the animals and their byproducts.

Thirty five complaints have been received on acaricides not killing ticks from farmers, drug shop operators, and field veterinarians. The President through the Office of the Prime Minister directed in April 2016 a policy review to solve the issue of resistance of ticks to acaricides within three months.

Recently the Executive Director NDA convened and facilitated initiation of a task force on tick resistance to acaricides. This taskforce is chaired by Ministry of Agriculture, Animal Industry and Fisheries(MAAIF) and NDA is the secretariat, with the National Livestock Resources Research Institute (NaLIRRI), State House representative, and Makerere University College of Veterinary medicine Animal resources and Bio-security as members. The task force looks into proposals of re-instating acaricide rotation in the country or import control, restriction of use of combination acaricides, other tick control measures like vaccination against ticks and tick borne diseases. The task force is yet to come up with the final recommendations

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8 FUTURE DIRECTION

8.1 Establish active Pharmacovigilance system for Bedaquiline for TB.

New TB drugs such as Bedaquiline, and others in the pipeline, are used in combination with existing antiTB drugs, creating a potential for previously unrecognised adverse events and drug interactions. Pharmacovigilance is thus an important part of global and national policy for addressing the safety of current and new anti TB drug regimens. Appropriate mechanisms have to be in place to report safety concerns alongside the monitoring of effectiveness.

Bedaquiline will be monitored actively and all activities will be integrated in the existing structures at all levels.

8.2 Active monitoring of the HPV vaccine Gardasil®

The HPV Vaccine currently rolled out by Uganda ministry of health will be monitored closely following a possibility of association of Postural Orthostatic Tachycardia Syndrome. Postural Orthostatic Tachycardia Syndrome (PoTS) is an abnormality of functioning of the autonomic (involuntary) nervous system. It is defi ned as an increase in heart rate of over 30 beats per minute (or to higher than 120 beats per minute) (40 bpm in those age 12-19) when standing upright. Typically there is no postural fall in blood pressure, although fainting (syncope) can occur (see below).

One case of possible PoTS has been reported in Uganda but earlier on a number of PoTS were reported in the Denmark ADR reports. The European Medicines Agency, EMA, investigated POTS as a possible adverse reaction to the HPV vaccine.

The Pharmacovigilance Risk Assessment Committee of EMA in their annual review of the safety of the HPV vaccine Gardasil®, concluded that at the time it was not possible to confirm or disprove that there is a causal relationship between Gardasil® vaccination and the occurrence of POTS. The NPC will be evaluating the possibility of this signal in Uganda.

8.3 Anti-Microbial resistance National taskforce

NDA is part of the Anti-microbial Resistance Taskforce that is drafting a National Anti-Microbial Resistance (AMR) Monitoring Plan in collaboration with a number of various stakeholders, an effort coordinated by Central Public Health Laboratories.

8.4 Patient involvement in ADR reporting.

The rate of reporting suspected Adverse Drug Reactions (ADRs) for Uganda is 20 per million inhabitants yet WHO recommends 200 per million inhabitants. This low rate of reporting affects our ability to detect signals of any drug related problem.

Many countries have allowed patients to start direct reporting ADRs after realizing its benefit. Recent studies have shown that patient reports can highlight important signals which could have been left out by the healthcare professionals. The national Pharmacovigilance centre will be launching an e- reporting platform as a mechanism to improve reporting in the country.

9 Recognition of Performance

In a special way, we would like to acknowledge the following health facilities and health workers for their excellent performance as regards reporting of ADRs based on criteria of number of reports, timeliness, and consistency;

Health facilities

1. Uganda cares, Masaka
2. Mubende Regional Referral Hospital
3. Fort portal Regional Referral Hospital (Sustain)

Regional Co-ordinators

1. Okello Harriet (Arua)
2. Dr. Patrick Musinguzi (Mubende)
3. Rodney Tibaruha (Kabale)

Health workers

1. Habib Hussein (Medical Clinical Officer, Uganda Cares, Masaka Hospital)
2. Kenneth Natuhwera (Pharmacy technician, Fortportal RRH)
3. Kiyingi Benon (Pharmacy technician, Bwizibwera HC IV)

FEATURE

ADVERSE EVENTS REPORTED ON TENOFOVIR BASED REGIMEN

In 2009 Tenofovir (TDF) was recommended as part of the alternative first-line ART regimen in the national ART guidelines. Use of Tenofovir by patients with mild renal dysfunction and/or use for longer durations might be associated with renal toxicity, as suggested by animal studies.

National Drug Authority through its Pharmacovigilance system has collected about 2279 adverse drug reaction (ADR) reports since 2006. This report provides information on adverse events experienced by patients using Tenofovir based regimen in Uganda, as reported by various health professionals through the spontaneous system to the National Pharmacovigilance Center (NPC) based in National Drug Authority (NDA).

Description of data

By April 2016, 157 individual case reports associated with Tenofovir were received. The reporting rate has been increasing over the years as indicated in figure 1.

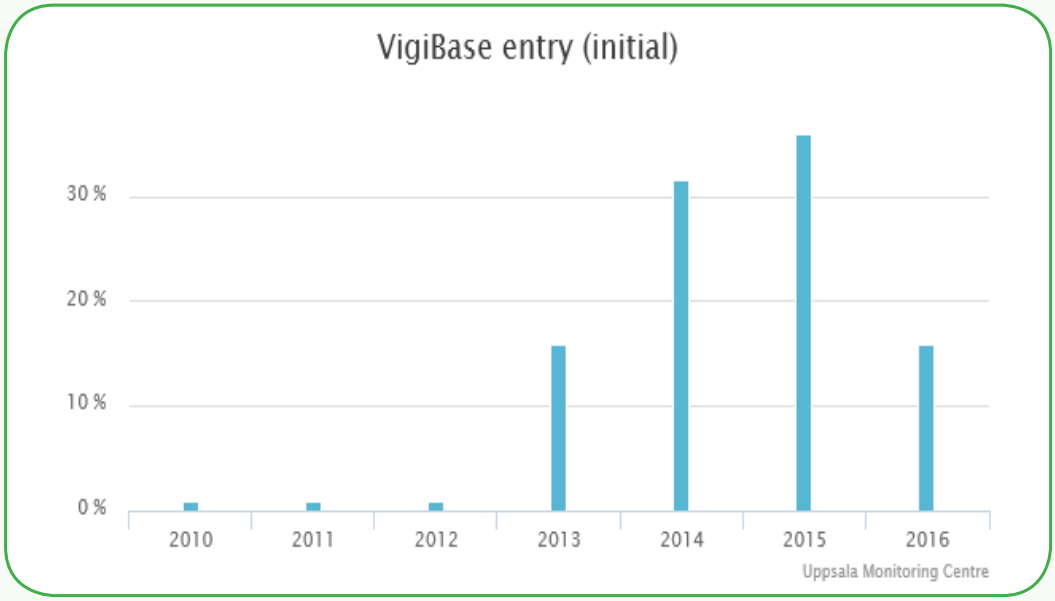


Figure 1 Distribution of Tenofovir reports over years

Out of the total reports on Tenofovir, 123 (78%) were suspected to be associated with renal dysfunction while the rest were associated with skin reaction and GIT disorders. Cases reported to be serious were 100(81%) with 2 cases of death being reported.

Presenting signs and symptoms for the suspected renal toxicity

Out of the 123 cases with suspected renal toxicities, 106(86.1%) presented with raised serum creatine of greater than >1.3 mg/dL followed by cases of musculo-skeletal disorders (characterized by bone demineralization, gait and hip joint pain, fractures) which were twelve (9.7%). Various reactions reported are shown in table 1 below.

Table 1: Presenting signs and symptoms of suspected renal toxicity

Reaction	No. of patients	Percentage %	Duration on treatment	Duration on treatment	Duration on treatment
			<1 year	1-2 years	>2 years
Serum creatinine >1.3 mg/ dL(Asymptomatic)	106	78	16	38	52
Facial puffiness/edema	6	4.87	1	4	1
Proteinuria	9	7.1	2	3	4
Glycosuria	1	0.8	0	0	1
Proteinuria and glycosuria	3	2.4	2	0	1
facial puffiness with Proteinuria	2	1.6	1	1	0
Musculo-skeletal disorders(bone demineralization/fractures/hip pain)	12	9.75	2	4	6
Bilateral pedal edema	7	5.69	0	4	2
Fanconi syndrome	5	4	1	2	2
	123	100	25	55	69

Cases with co-morbidities

Nine cases had co-morbidities of both hypertension and diabetes mellitus .Other co-morbidities reported included one case of lipodystrophy and one case of Kaposi's sarcoma.

Intervention done

Fifty three patients (42%) were changed to a non-Tenofovir-based regimen as presented in the figure 2.

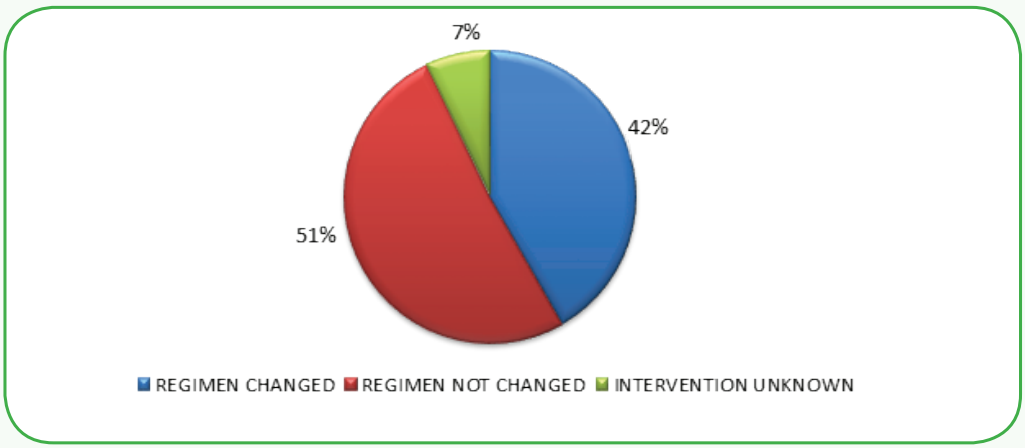


Figure 2 Intervention done for patients with suspected adverse reactions

Comparisons with global statistics

Globally, 97661 individual case reports have been submitted to the WHO global database with Americas reporting the most on Teneofovir as shown in the figure 3 below.

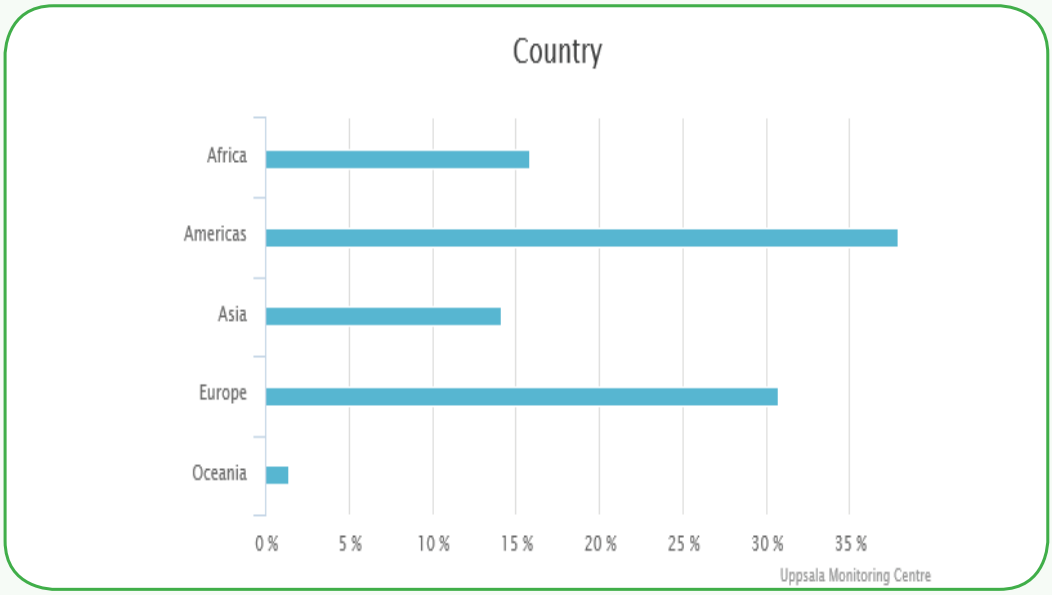
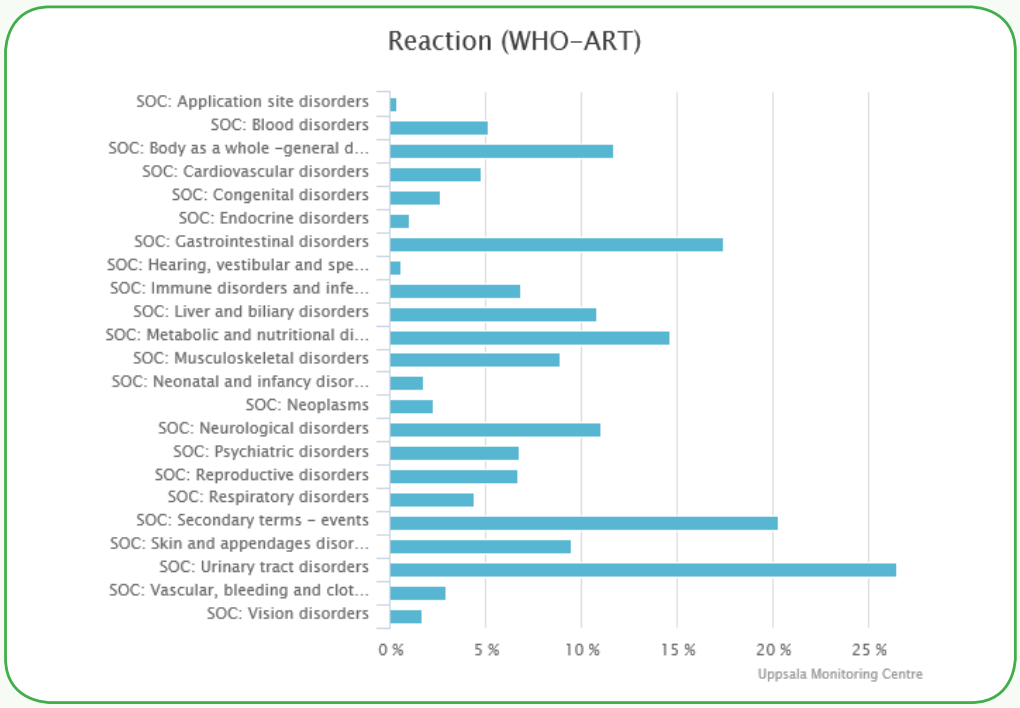


Figure 3 Global reporting rates

At a global level, most reported reactions associated with Tenofovir is shown is figure 4 below.



Discussion

Clinical trial data suggest that risk of TFV renal toxicity is low (approximately 1%) in selected patients with good dosing practices and vigilance in patient monitoring (Szczech, 2008). Some observational studies suggest a higher risk, given that patients' populations are more heterogeneous and treatment is more complex in real life. As the country continues to use TDF- based regimen monitoring of patients in order to improve care and safety of patients on antiretroviral therapy in Uganda through early detection of renal toxicity in TFV based regimen is very critical.

Limitations of the data

The data presented is based on spontaneous reporting which presents limitations that are mainly related to under-reporting, variable quality of the reported data and lack of information on drug exposure.

The likelihood of a causal relationship is not the same in all reports. Any use of this information must take these factors into account.

Recommendations

Aids control program to deliberately put effort in sensitizing clinicians and provide the necessary infrastructure needed to screen patients who are at risk of getting and monitor toxicities related to use of TDF to permit more timely diagnosis and management.

ANNEX: PHARMACOVIGILANCE REGIONAL COORDINATORS

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