Analysis of Passive Surveillance Data Collected by the Swaziland Pharmacovigilance Unit, October 2016–March 2017

July 2017

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ANALYSIS OF PASSIVE SURVEILLANCE DATA COLLECTED BY THE SWAZILAND PHARMACOVIGILANCE UNIT, OCTOBER 2016–MARCH 2017

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July 2017

This report is made possible by the generous support of the American people through the US Agency for International Development (USAID), under the terms of cooperative agreement number AID-OAA-A-11-00021. The contents are the responsibility of Management Sciences for Health and do not necessarily reflect the views of USAID or the United States Government.

About SIAPS

The goal of the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program is to ensure the availability of quality pharmaceutical products and effective pharmaceutical services to achieve desired health outcomes. Toward this end, the SIAPS result areas include improving governance, building capacity for pharmaceutical management and services, addressing information needed for decision-making in the pharmaceutical sector, strengthening financing strategies and mechanisms to improve access to medicines, and increasing quality pharmaceutical services.

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Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. 2017. *Report of Analysis of Passive Surveillance Data Collected by the Swaziland Pharmacovigilance Unit, October 2016–March 2017.* Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program. Arlington, VA: Management Sciences for Health.

Key Words

Spontaneous reporting, passive surveillance, adverse drug reactions, pharmacovigilance

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CONTENTS

ACRONYMS

3TC	lamivudine
ABC	abacavir
ADR	adverse drug reaction
ART	antiretroviral therapy
ARV	antiretroviral
ATV/r	atazenavir boosted with ritonavir
AZT	zidovudine
CS	cycloserine
CTX	cotrimoxazole/trimethoprine
D4T	stavudine
DD	drug dictionary
EFV	Efavirenz
HCTZ	hydrochlorothiazide
ICH	International Conference on Harmonization
INH	isoniazide
KM	kanamycine
LFX	levofloxacin
LPVr	lopinavir boosted with ritonavir
MDR-TB	multidrug-resistant TB
NPVU	National Pharmacovigilance Unit
NVP	nevirapine
PAS	para amino salicylic acid
PTO	prothionamide
PV	pharmacovigilance
PViMS	Pharmacovigilance Monitoring System
RHE	rifampicine/isoniazid/ethambutol
RHZE	rifampicine/isonaizid/pyrizinamide/ethambutol
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
TB	tuberculosis
TDF	tenofovir
TTO	time to onset
USAID	US Agency for International Development
WHO	World Health Organization
XDR-TB	extremely drug resistant TB
Z	Pyrizinamide

EXECUTIVE SUMMARY

Background

With support from the US Agency for International Development (USAID)-funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program, implemented by Management Sciences for Health, the Swaziland National Pharmacovigilance Unit (NPVU) has been monitoring the safety of medicines used in the county by collecting and collating reports of adverse drug reactions (ADRs) and other medicine-related problems through its spontaneous reporting system established under the country's Ministry of Health in 2009. In addition, SIAPS has been supporting active surveillance for antiretroviral (ARV) and tuberculosis (TB) medicines.

ADRs and other medicine-related problems are reported to the NPVU by health care providers using a paper ADR reporting form. Completed forms are sent to the NPVU or collected from health care facilities on a quarterly basis for data entry and analysis. SIAPS supports the collection of the forms and has seconded a data clerk to the NPVU to enter data from the forms into a Microsoft Excel database.

SIAPS support was further sought to analyze pharmacovigilance (PV) data and build the capacity of the PV team to undertake routine analysis of those data.

Objectives

The main objective was to analyze PV data generated from the spontaneous reporting system in Swaziland to inform clinical practice (rational medicine use) and improve patient outcomes.

Methods

We undertook a review of the retrospective data on ADRs and other medicine-related problems collected by the NPVU through the spontaneous reporting system between October 2016 and March 2017.

All completed ADR report forms sent to the NPVU within the period under review were collated and entered into a Microsoft Excel database for analysis. Data were analyzed with descriptive statistics to determine the demographic characteristics of patients, most frequently reported suspected medicines and ADRs, and distribution of reporters by professional cadre. Any association between groups was determined using Chi-square tests.

Key Findings

- Of the reports in the database, 96.0% met the minimum validity requirements and were included in the analysis.

- Reports in the database were evenly distributed between male and female patients.
- The average patient age was 37 years.
- A total of 44 medicines, either in combination or as a single entity, were suspected of causing 307 ADRs and or other medicine-related problems, and 70 distinct reactions were recorded.
- ARVs were the most common medicines in the database, with the TDF/3TC/EFV and TDF/3TC/NVP combinations having the highest counts.
- Antiretroviral therapy (ART) accounted for 54.0% of the reported indications for use of suspected medicines in the reports.
- A total of 70 types of ADRs were reported. Gynecomastia was the most frequent at 15.3%, followed by rashes at 13.0%.
- There was a significant association between the number of medicines and the number of ADRs in a report.
- Of the ADRs reported, 12.8% resulted in hospitalization and 4.3% were life threatening.
- Of the reactions, 75.8% were minor and 5.9% were major, while 0.5% were product use error.
- Three cases each of death and persistent disability were recorded, 71.3% of patients had not recovered at the time of reporting, and 23.8% had fully recovered.
- Doctors reported the majority of cases, followed by pharmacy technicians.
- No reports were received directly from patients/consumers.

Key Recommendations

The recommendations from this work are two-fold: those aimed specifically at strengthening the NPVU and those aimed at strengthening the larger health care system to improve treatment outcomes.

NPVU Targeted Recommendations

- The NPVU demonstrated good capacity to collect and collate reports from the spontaneous reporting system. There is a need to encourage direct data entry into existing ADR data management software, such as the Pharmacovigilance Monitoring System (PViMS) and VigiFlow, which are already being used by the NPVU. This will ensure proper coding of ADRs and medicines using internationally accepted standard dictionaries, such as MedDRA and the World Health Organization (WHO) Drug Dictionary (DD), that are built into the

software. These programs also make it possible to provide separate and complete information on suspected medicines as well as concomitant medicines used by patients. This will improve data management and facilitate routine data analysis.

- The NPVU should consider harmonizing the categorizations for severity, seriousness, and outcomes with the WHO or International Conference on Harmonization (ICH) categorization as appropriate.

- A large number of reports provided complete and useful information. However, some did not provide critical information required for proper causality assessment, such as dates of medicine use and ADR onset, which indicates the need for the NPVU to further educate reporters.

- The NPVU needs to be strengthened to routinely undertake causality/relationship assessments on collected ADR reports, such as through a work sharing mechanism with members of the Advisory Committee. The results of the causality assessment are necessary for providing meaningful feedback on the reports.

- Health care providers have shown a willingness to participate in the PV system by providing quality information related to medicine use. This momentum should be maintained by providing specific feedback to reporters from the results of the analysis through existing stakeholder feedback forums. This will encourage further reporting of ADRs and other medicine-related problems.

- The NPVU should be supported to establish a system for direct patient reporting of ADRs and other medicine-related problems.

Health-system Related Recommendations

- The majority of the reports were on ARVs. Reporting of other medicines used in the health care system should be promoted. Expanded support should be provided to ensure the reporting of ADRs and medicine-related problems beyond ARVs.

- Health care providers need to be sensitized on medication error issues and the need to report such occurrences.

- Reporting by doctors was very high. However, reporting by pharmacists and nurses was very low. This shows the need to get pharmacists, nurses, and possibly other health care providers more involved in the spontaneous reporting system through education on and awareness of PV.

- Reporting of ADRs and other medicine-related problems should be expanded to include health care providers in the private sector and those at lower levels of health care delivery by training them and actively engaging them in the PV process.

INTRODUCTION

With support from SIAPS, the Swaziland NPVU has been monitoring the safety of medicines used in the county by collecting and collating reports of ADRs and other medicine-related problems through its spontaneous reporting system established under the country's Ministry of Health in 2009. In addition, SIAPS has been supporting active surveillance for ARV and TB medicines.

ADRs and other medicine-related problems are reported to the NPVU by health care providers using a paper ADR reporting form. Completed forms are sent to the NPVU or collected from health care facilities on a quarterly basis for data entry and analysis. SIAPS supports the collection of the forms and has seconded a data clerk to the NPVU to enter the data from the forms into Microsoft Excel.

SIAPS support was further sought to analyze PV data and build the capacity of the PV team to undertake routine analysis of those data.

OBJECTIVES AND METHODS

Objective

The main objective of the work was to analyze PV data generated from the spontaneous reporting system in Swaziland to inform clinical practice (rational medicine use) and improve patient outcomes.

Specific objectives were to:

- Characterize patients most affected in terms of age, weight, and gender
- Determine the medicines or medicine combinations most frequently involved in ADR reports in the database, including the indications for use, route of administration, and number of medicines per report.
- Identify the most frequently reported ADRs, including the severity, time to onset of reaction, category of ADR, and outcome of the reactions.
- Determine the distribution of reporters by professional cadre

Method

We undertook a review of retrospective data on ADRs and other medicine-related problems collected by the Swaziland PV Unit between October 2016 and March 2017. Primary data are routinely collected using an ADR report form. Health care providers are encouraged to provide basic information on four main elements considered the minimum reporting requirements: the patient, the suspected medicine(s), the suspected reaction(s), and an identifiable source of report (reporter). A report is generally considered valid if it has minimum information on all of the following:

- An identifiable patient (identified by initials, gender, and/or age)
- A suspect medicine (brand and/or generic name); route of administration and/or start and stop dates of administration should also be provided if available
- A description of at least one suspected ADR
- A source of report/reporter (identified by name, profession, institution, and/or contact information)

On the Swaziland ADR report form (annex A), only one space is provided for information on medicines. When information on more than one medicine is provided, reporters are advised to circle the suspected medicine.

All ADR report forms sent to the NPVU between October 2016 and March 2017 were collated, and the data were entered into Microsoft Excel.

Data Cleaning and Extraction

The data were cleaned to remove duplicate and invalid reports. Duplicate reports are reports that have identical information on the same patient (identified by both initials and age). Invalid reports did not contain the minimum required information. However, two reports did not have any information on the source of report (i.e., no name, profession, institution, or contact information of reporter) but were included in the analysis because the omission was not considered critical.

The valid reports were exported to IBM SPSS® version 21 software for data analysis.

Data Analysis

The data were analyzed using descriptive statistics to determine percentages/frequencies for string and categorical variables, while means, minimum and maximum values, and standard deviation were determined for continuous variables. The Pearson Chi-square test was used to compare the difference between groups and test for any association. Parameters analyzed were gender, age, weight, and pregnancy status of patients; suspected medicine and concomitant medicines; route of administration and indication for use of suspected medicine; first, second, and third reported ADRs; number of patients that had one or more ADRs and average number of ADRs per patient; time to onset (TTO) of ADR; severity and category of reported ADRs (as classified on the Swaziland ADR form); outcome of ADR; and profession (cadre) of reporters. The results of the analysis are presented below.

RESULTS

A total of 225 reports on ADRs and other medicine-related problems were entered into the database within the reporting period. Of these reports, 216 (96.0%) were considered valid and retained for data analysis.

Patient Demographics

Gender/Pregnancy Status

Patient gender was included in 213 reports, while three reports did not contain that information. Reports were evenly distributed between male and female patients, with 50.2% (107) being on male patients and 49.8% (106) on female patients (table 1).

Of the 106 reports on female patients, 84 had information on pregnancy status. Of these, 98.0% (82) of patients were reported as not pregnant while 2.0% (2) were reported as pregnant.

Table 1. Distribution of Reports by Gender

Gender	Frequency	Percentage	Valid Percentage
Male	107	49.5	50.2
Female	106	49.1	49.8
Total	213	98.6	100.0
Missing	3	1.4	
Total count	216	100.0	

Age and Weight

Information on either the age or birth date of the patient was found in 211 reports. The mean age for patients was 37 years (minimum 1 year, maximum 84 years). The standard deviation was 16.

Similarly, 176 reports had information on patients' weight. The mean weight was 60.5 kg (minimum 8 kg, maximum 107 kg). The standard deviation was 19.

Suspected/Concomitant Medicines/Route of Administration/Indication for Use

Suspected Medicine/Number of Medicines in Report

Of the 216 reports, 156 (72.0%) included more than one medicine, but only 53 (34.0%) of these indicated the suspected medicine. For our analysis, if the suspected medicine was not indicated, the first medicine listed was assumed to be the suspect medicine; this was carefully crosschecked against the reported indication for use where available. When a report contained only one medicine, it was as assumed to be the suspected medicine.

All of the analyzed reports had one or more medicines either in combination or as a single entity. For this analysis, combination medicines such as ARVs were considered to have more than one medicine. Among the reports, 60 (27.78%) had only one suspected medicine, 81 (37.5%) had two to three medicines, and 75 (34.7%) had more than three medicines. There was no statistically significant difference (p=0.137) between male and female patients in the number of medicines contained per report.

A total of 44 different medicines, either in combination or as single entities, were reported, with the largest number of reports being on the ART combination TDF/3TC/EFV. Figure 1 shows the distribution of the top 10 suspected medicines in the database. The full list and distribution of all suspected medicines in the reports can be found in annex B.

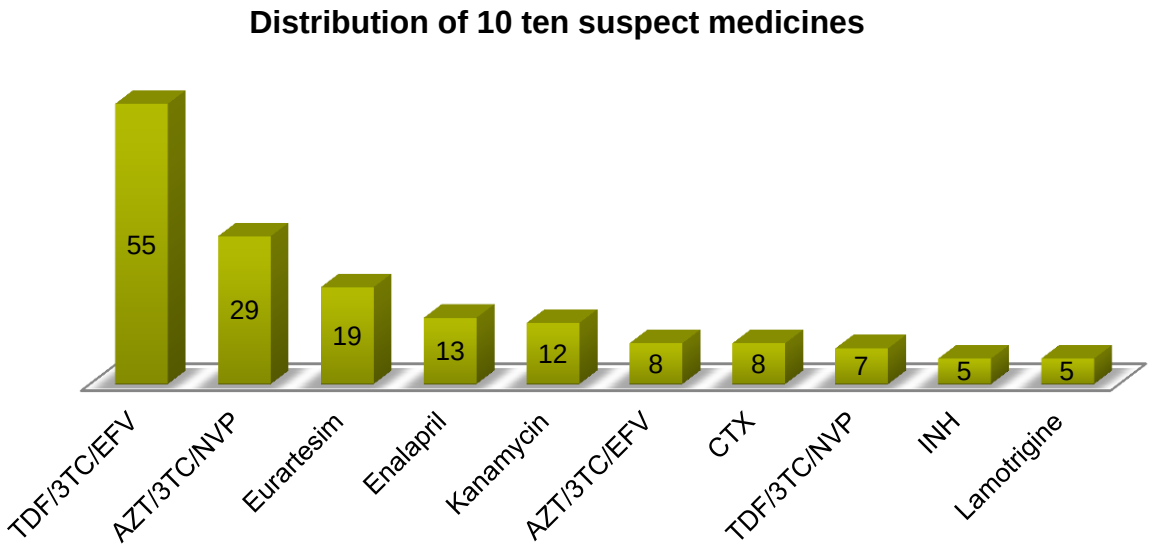

Figure 1. Distribution of the top 10 suspected medicines in the ADR database

Route of Administration/Indication for Use

Information on the route of administration of the suspected medicine was included in 203 reports (94.0%), with 190 (93.6%) of those indicating oral administration and 13 (6.4%) indicating intramuscular administration.

Similarly, 203 reports (94.0%) had information on the indication for use of the suspected medicine. ART accounted for 54.2% (110 reports) of the indication for use of the medicines, followed by hypertension and prevention of malaria with 9.4% (19 reports) each. Figure 2 gives a graphic representation of the top eight indications for use of the suspected medicines in the reports. A complete listing of all indications for use of the suspected medicines in the database can be found in annex B.

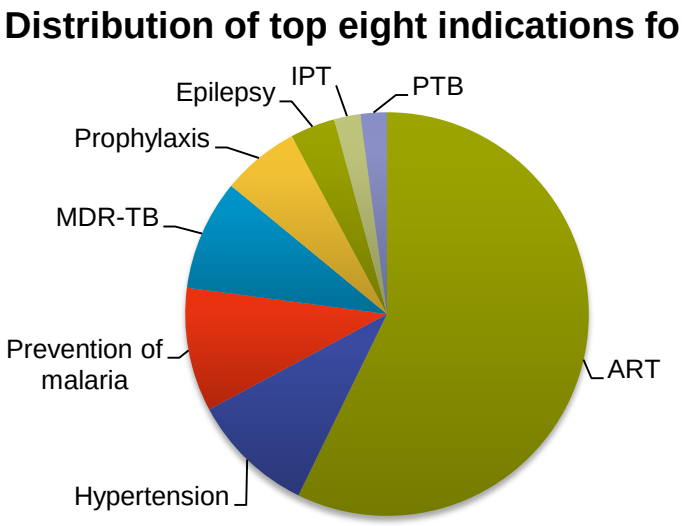

Figure 2. Distribution of the top eight indications for use of suspected medicines

Suspected Adverse Drug Reactions

All 216 reports contained information on at least one suspected ADR, with 158 reports (73.1%) containing only one suspected ADR, 49 (22.7%) containing two to three, and 9 (4.2%) containing more than three. There was no statistically significant difference (p=0.539) between male and female patients in the number of suspected ADRs per report.

Frequency and Types of Reactions

The suspected ADRs were not coded by system organ class in the database. Therefore, to simplify the analysis, some of the descriptions for suspected ADRs were coded using similar terms. For example, descriptive terms such as enlargement of the left and/or right breast or bilateral breast enlargement were coded "gynecomastia"; all reports with any description of rash that contained the word rash were coded "rashes"; all descriptions of cough (e.g., persistent coughing, dry cough) were coded "cough"; all joint-related terms (e.g., knee pain, bilateral ankle pain) were coded "arthralgia"; and terms such as renal insufficiency, renal failure, hepatitis, and rise of hepatic enzymes were coded "renal dysfunction". Based on this coding system, 70 unique ADRs were recorded. Table 2 shows the distribution of the first reported suspected ADR in the reports.

A total of 307 suspected ADRs and/or other medicine-related problems encompassing the 70 distinct reaction types were documented in the reports for both suspected and concomitant medicines. Gynecomastia was the most frequently reported suspected ADR at 15.3% (33) of reported cases, followed by rashes at 13.0% (28) of reported cases. There was a statistically significant association (p=0.013) between the number of medicines in a report and the number of ADRs reported by patients. Table 3 gives the result of cross tabulation of number of suspected medicines with number of ADRs in a report.

Table 2. Distribution of First Reported ADR

Description of ADR	Frequency	Valid Percentage
Gynecomastia	33	15.3
Rashes	28	13.0
Renal dysfunction	15	6.9
Cough	13	6.0
Anemia	11	5.1
Lipodystrophy	10	4.6
Abdominal pain	8	3.7
Angioedema	8	3.7
Arthralgia	7	3.2
Immunological failure	7	3.2
Dizziness	6	2.8
Peripheral neuropathy	5	2.3
Tinnitus	5	2.3
Hearing loss	4	1.9
Jaundice	4	1.9
Psychosis	4	1.9
Headache	3	1.4
Itching	3	1.4
Nausea	3	1.4
Treatment failure	3	1.4
Hypokalemia	2	.9
Hypothyroidism	2	.9
Malaise	2	.9
Toxic epidermal necrolysis	2	.9
Vomiting	2	.9
Abdominal discomfort	1	.5
Allergic reaction	1	.5
Burning sensation of hands and feet	1	.5
Chest tightness	1	.5
Chills	1	.5
Confusion	1	.5
Cramps	1	.5
Depression	1	.5
Diarrhea	1	.5
Dry mouth	1	.5
Foggy vision	1	.5
Hallucination	1	.5
Hepatitis	1	.5
Hypersensitivity reaction	1	.5
Loss of energy	1	.5
Lymphadenopathy	1	.5
Pain	1	.5
Palpitation	1	.5
Pancytopenia	1	.5
Poor appetite	1	.5
Steven Johnson Syndrome	1	.5
Tremors	1	.5
Twisting of neck	1	.5
Ulceration and blisters on lips and mouth	1	.5
Weakness	1	.5
Yellow eyes	1	.5
Total valid count	216	100.0

Time to Onset of Reaction

Of the reports analyzed, 159 (73.6%) had sufficient information to enable the TTO of reaction to be calculated (i.e., the date the suspected medicine was started and the date the suspected ADR started). The average TTO was calculated to be approximately 575.73 days (82 weeks). The minimum TTO was 0 days and the maximum was 3,643 days (520 weeks).

Severity, Category, and Outcome of ADR

On the Swaziland ADR form, severity is classified as life threatening, hospitalized, and not hospitalized. Severity was indicated on 188 reports (87.0%), with 156 (83.0%) cases not hospitalized, 24 (12.8%) hospitalized, and 8 (4.3%) being life threatening (figure 3).

A total of 186 reports (86.1%) categorized the ADR, with 141 (75.8%) categorized as suspected minor, 11 (5.9%) as suspected major, and 1 (0.5%) as product use error (figure 4).

Similarly, information on outcome of the reaction was available for 122 (56.5%) reports. Of these, 87 (71.3%) patients had not recovered at the time of reporting and 29 (23.8%) had fully recovered. Three (2.5%) patients died as a result of the ADR and another three had a persistent disability (figure 5).

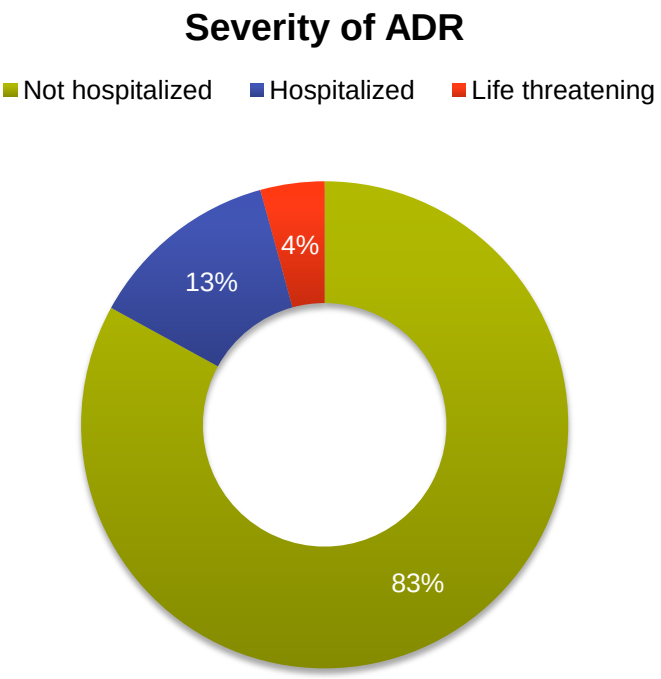

Figure 3. Distribution of reports in database by severity of ADR

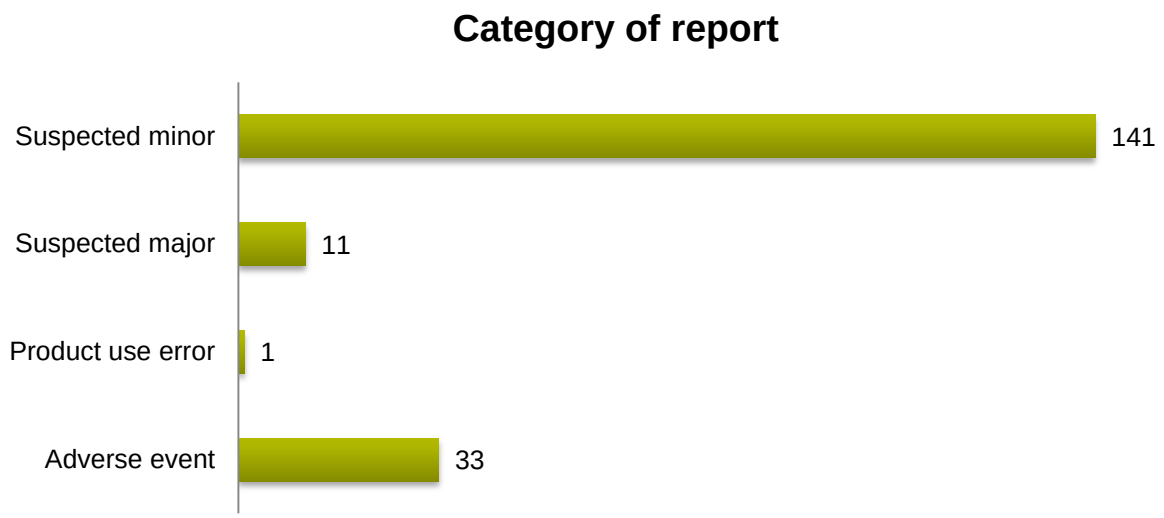

Figure 4. Distribution of reports in the database by category of report

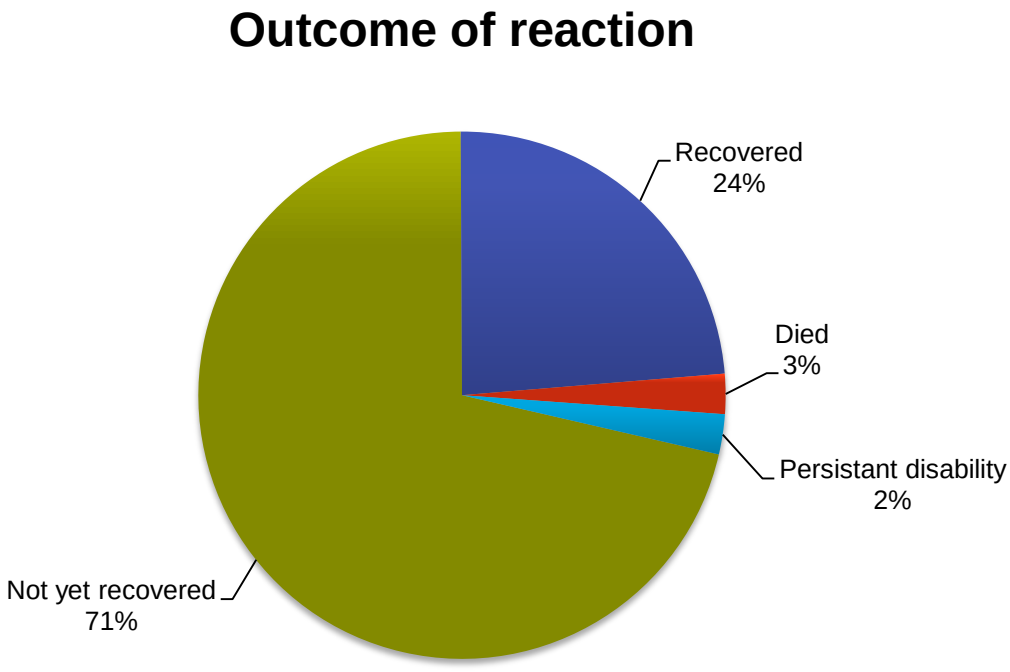

Figure 5. Outcome of reactions in the ADR reports

Sources of Reports (Reporter Information)

The source of the report was provided in 210 (97.2%) reports. The majority of reports (104, 49.5%) were sent by doctors, followed by pharmacy technicians (45, 21.4%), nurses (41, 19.5%), and pharmacists (20, 9.5%) (figure 6).

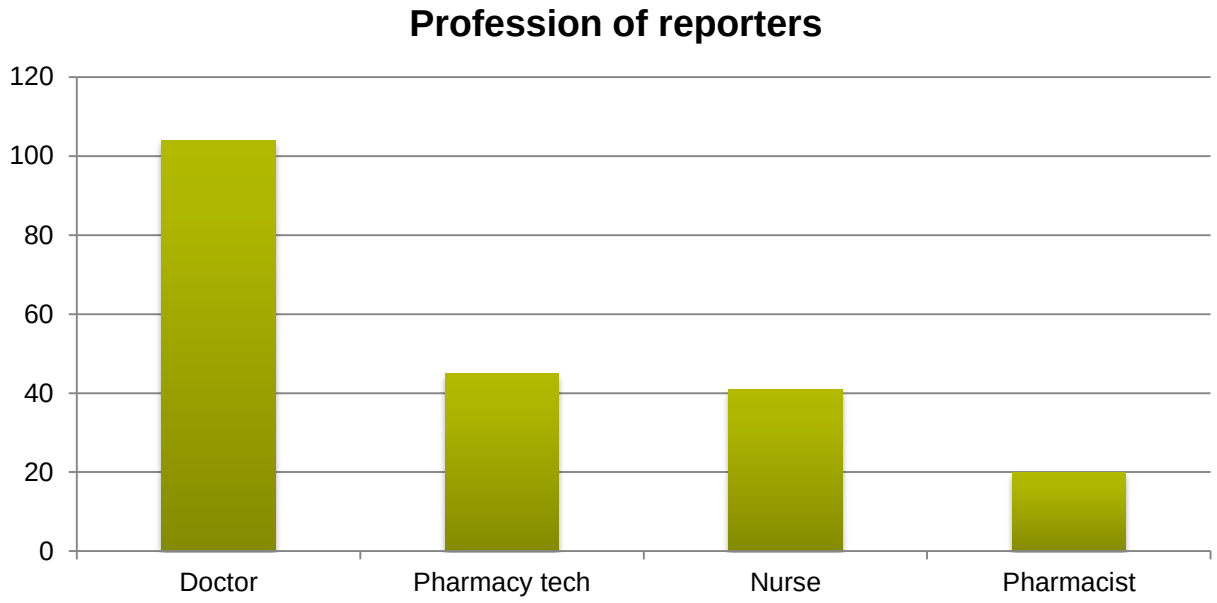

Figure 6. Profession of sources of report (reporters)

Table 3. Cross-tabulation of Number of Medicines in Report and Number of Reported ADRs

			Number of reported ADRs			
			One ADR	Two or three ADRs	More than three ADRs	Total
Number of medicines in report	One suspected medicine	Count	36	19	5	60
		% within number of medicines in report	60.0%	31.7%	8.3%	100.0%
		% within number of reported ADRs	22.8%	38.8%	55.6%	27.8%
	Two or three suspected medicines	Count	69	11	1	81
		% within number of medicines in report	85.2%	13.6%	1.2%	100.0%
		% within number of reported ADRs	43.7%	22.4%	11.1%	37.5%
	More than three suspected medicines	Count	53	19	3	75
		% within number of medicines in report	70.7%	25.3%	4.0%	100.0%
		% within number of reported ADRs	33.5%	38.8%	33.3%	34.7%
Total		Count	158	49	9	216
		% within number of medicines in report	73.1%	22.7%	4.2%	100.0%
		% within number of reported ADRs	100.0%	100.0%	100.0%	100.0%
P=0.013						

SUMMARY OF KEY FINDINGS

PV aims to achieve the best outcome from treatment with medicines. This can be accomplished through several means, including the spontaneous reporting system. The objectives of this system include detecting problems related to medicine use and communicating the findings in a timely manner, contributing to the assessment and communication of risks and benefits of medicines on the market, improving rational and safe medicine use, and educating and providing information to consumers (health care providers and patients) about medicines. This can only be achieved when locally generated data are used to inform locally relevant decision making. The routine and timely assessment of data collected through the spontaneous reporting system therefore becomes critical to the effective functioning of a PV system. This analysis was undertaken to use evidence generated from the data to improve local practice. Key findings from the analysis are outlined below, along with recommendations on how to improve the system.

In spontaneous reporting, denominator data (number of those who have taken a particular medicine) is often not known or incomplete at best. Therefore, when interpreting these findings, it is important to note that the figures represent absolute values rather than rates (such as relative risks).

- In general, a very large number of reports in the database (96.0%) met the minimum requirements for a valid report and could contribute to efforts to improve the system.

- There was an even distribution between male and female patients in the reports contained in the database, and the average patient age was 37 years.

- A total of 44 medicines, either in combination or as a single entity, were suspected of causing ADRs or other medicine-related problems.

- ARVs were the most frequently suspected medicines in the database, with the TDF/3TC/EFV and TDF/3TC/NVP combinations having the highest and second-highest counts, respectively.

- Among the reports, 37.5% had two to three medicines and 34.7% had more than three medicines.

- There was no statistically significant difference between males and females in the number of medicines per report.

- ART was by far the most frequent indication for use of suspected medicines in the reports, at approximately 54.0%.

- A total of 70 unique types of ADRs were reported. Gynecomastia was the most frequently reported suspected ADR (15.3%), followed by rashes (13.0%).

- There was a significant association between the number of medicines and the number of ADRs in a report.

- The average TTO of ADR was calculated at 575.73 days, equivalent to 82 weeks (20.5 months).

- Among the reported ADRs, 12.8% resulted in hospitalization of the patient and 4.3% were life threatening.

- The majority of reported ADRs (75.8%) were minor, while 5.9% were major and 0.5% were product use errors.

- Three cases each of death and persistent disability were recorded, 71.3% of patients had not recovered at the time of reporting, and 23.8% had fully recovered.

- Doctors submitted the majority of reports, followed by pharmacy technicians and nurses. Pharmacists submitted the fewest number of reports.

- No ADR reports were received directly from patients/consumers.

RECOMMENDATIONS

The recommendations in this report will assist those seeking to improve operations of the NPVU and those working to strengthen the health care system and improve treatment outcomes. Some of these recommendations were also drawn from experiences during the analysis.

NPVU-related Recommendations

- The NPVU has demonstrated good capacity to collect and collate reports from the spontaneous reporting system. Direct data entry into existing ADR data management software, such as PViMS and VigiFlow, already being used by the NPVU is encouraged to ensure proper coding of ADRs and medicines into internationally accepted standard dictionaries, such as MedDRA and WHO-DD, that are built into the software. These programs also make it possible to provide separate and complete information on both suspected medicines and concomitant medicines used by patients.

- The NPVU should consider harmonizing the categorizations for severity, seriousness, and outcome with the WHO or ICH categorization as appropriate.

- A large number of reports provided complete and useful information, but some did not provide critical information required for proper causality assessment, such as dates of medicine use and ADR onset, indicating the need for the NPVU to further educate reporters.

- The NPVU should be strengthened to routinely undertake causality/relationship assessment on collected ADR reports, such as through a work-sharing mechanism with members of the Advisory Committee. Results of the causality assessment are necessary for providing meaningful feedback on reports.

- Health care providers have shown willingness to participate in the PV system by providing quality information related to medicine use. This momentum should be maintained by providing specific feedback to reporters on the results of the analysis through existing stakeholder feedback forums. This will encourage further reporting of ADRs and other medicine-related problems.

- The NPVU should be supported to establish a system for direct patient reporting in line with the current global practice of encouraging direct reporting of ADRs and other medicine-related problems by patients/consumers.

Health System-related Recommendations

- The majority of the reports were on ARVs. Reporting of other medicines used in the health care system should be encouraged. Expanded support should be provided to ensure reporting of ADRs and other medicine-related problems beyond ARVs.

- Health care providers need to be sensitized on medication error issues and the need to report such occurrences.

- Reporting of ADRs by doctors was very high. In comparison, reporting by pharmacists and nurses was very low. This shows the need to get pharmacists, nurses, and other health care providers more involved in the spontaneous reporting system through education and awareness of the importance of PV.

- Reporting of ADRs and other medicine-related problems should be expanded to include health care providers in the private sector as well as those at lower levels of health care delivery by training and actively engaging them in the PV process.

RESOURCES

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ANNEX A. SWAZILAND ADR REPORT FORM

MINISTRY OF HEALTH

Adverse Drug Reactions (ADR) Report Form

No: 15/ 1961

Report can be returned to **Central Medical Stores** "Attention" **Quality Control Pharmacist**
Fax: 2518 6279
Email: swazilandpharmacovigilance@gmail.com
For Further inquiries, please contact the Quality Control Pharmacist at Central Medical Stores at 2518 4111 or 2518 7255

Section (A): Patient Information

Patient initials:..... Gender: ☐ M ☐ F Pregnant? No ☐ Yes ☐ Unknown ☐

Weight (if known).....kg Date of birth: ...../...../..... Age: ☐

Section (B): Medication History

All Drug Therapies/Vaccines Prior to ADR (Please use trade names and circle the suspected drug.)	Batch number	Daily Dosage	Route	Date Begun	Date Stopped	Indication for use

Allergies or other relevant history (including medical history), liver/kidney problems, smoking, alcohol use etc)

Section (C): About the Adverse Drug Reaction

Date of onset of ADR: ...../...../.....

Description of event: _____

Category of ADR (please tick)

☐ Suspected minor / major reaction from a drug (e.g. allergic reaction) ☐ Adverse Event (e.g. congenital defects)
☐ Product Use Error (e.g. use of antibiotic instead of NSAID)

Severity (can tick more than one if appropriate):

☐ Life threatening ☐ Hospitalized date ...../...../..... ☐ Hospitalization NOT required

Relevant Laboratory result: _____

Section (D): Treatment & Outcome

Treatment of ADR: ☐ No ☐ Yes. Details (including dosage, frequency, route duration)

Outcome:

☐ Recovered on date ...../...../..... ☐ Not yet recovered ☐ Unknown ☐ Died on date: ...../...../.....
☐ Persistent disability ☐ Birth defect ☐ Medically significant events

Details: _____

Section (E): Report Details

Name:..... Sector of service:..... Private:..... Public:.....
Occupation:..... Doctor:..... Dentist:..... Pharmacist:..... Nurse:.....
Others:..... Correspondence Address:.....
Tel. No.:..... Fax: No:..... Email:.....
Also report to: Manufacturer:..... Distributor/Importer:..... Others:.....
Date of this report:...../...../20.....

FOR OFFICIAL USE ONLY

Report to: Manufacturer ☐ Distributor/Importer ☐ Other: ☐
Reported by:..... Capacity:.....

Instructions/Notes

1. ADR can briefly described as a noxious and unintended response to a drug or vaccine when the normal dose is used.
2. This report form is used for voluntary reporting of all suspected ADR.
3. There is no need to put down the full name of the patient.
4. Please provide information to every section. Information of individual reporter will be treated with strict confidence.
5. Please use another page for additional information if necessary.
6. Where date is required write in this format DD / MM / YYYY

"Completion of this form is not an admission of guilt or negligence"

ANNEX B. FREQUENCY TABLES

Following is a full listing of the frequency tables for all medicines (suspected and concomitant), ADRs, indications for use of the suspected medicines, and other parameters that were analyzed

	Patient gender	Frequency	Percentage	Valid Percentage	Cumulative Percentage
Valid	Male	107	49.5	50.2	50.2
	Female	106	49.1	49.8	100.0
	Total	213	98.6	100.0	
Missing	System	3	1.4		
Total		216	100.0		

	Suspected medicine	Frequency	Percentage	Valid Percentage	Cumulative Percentage
Valid	ABC/3TC/EFV	2	.9	.9	.9
	ABC/3TC/NVP	2	.9	.9	1.9
	AZT	1	.5	.5	2.3
	AZT/3TC/ATV/r	1	.5	.5	2.8
	AZT/3TC/EFV	8	3.7	3.7	6.5
	AZT/3TC/LPVr	1	.5	.5	6.9
	AZT/3TC/NVP	29	13.4	13.4	20.4
	Bactrim-Kid	1	.5	.5	20.8
	Capreomyclin/RHE/LVF/ INH	1	.5	.5	21.3
	Captopril	3	1.4	1.4	22.7
	Carbamazepine	3	1.4	1.4	24.1
	CTX	8	3.7	3.7	27.8
	D4T/3TC/NVP	2	.9	.9	28.7
	Dapsone	1	.5	.5	29.2
	Diclofenac	1	.5	.5	29.6
	EFV	1	.5	.5	30.1
	Enalapril	13	6.0	6.0	36.1
	Eurartesim	19	8.8	8.8	44.9
	Haldol	1	.5	.5	45.4
	HCTZ	1	.5	.5	45.8
	Hydrochlorothiazide	1	.5	.5	46.3
	INH	5	2.3	2.3	48.6
	Kanamycin	12	5.6	5.6	54.2
	KM/CS/LFX	1	.5	.5	54.6
	Lamotrigine	5	2.3	2.3	56.9
	Loperamide	2	.9	.9	57.9
	Measles vaccine	1	.5	.5	58.3
	Morphine syrup	2	.9	.9	59.3
	MR vaccine	1	.5	.5	59.7
	Nifedipine	2	.9	.9	60.6
	Omeprazole	1	.5	.5	61.1
	Phenobarbitone	2	.9	.9	62.0
	Praziquantel	3	1.4	1.4	63.4
	PTO	2	.9	.9	64.4
	Pyrazinamide	2	.9	.9	65.3
	RHZE	4	1.9	1.9	67.1
	Sirturo	1	.5	.5	67.6

	Suspected medicine	Frequency	Percentage	Valid Percentage	Cumulative Percentage
	TDF/3TC/EFV	55	25.5	25.5	93.1
	TDF/3TC/NVP	7	3.2	3.2	96.3
	Tegretol	1	.5	.5	96.8
	Tenolam E	4	1.9	1.9	98.6
	Tramadol	1	.5	.5	99.1
	Z/KM/LVF/PTO/cycloserine /pyridoxine/	1	.5	.5	99.5
	Z/LVF/etion/KM/CS/INH/ PAS	1	.5	.5	100.0
	Total	216	100.0	100.0	
Name of concomitant medicine-1					
Valid	Lasix	1	.5	1.1	1.1
	AZT/3TC/LPVr	1	.5	1.1	2.3
	AZT/3TC/NVP	2	.9	2.3	4.6
	CTX	40	18.5	46.0	50.6
	D4T/3TC/NVP	1	.5	1.1	51.7
	Dapsone	2	.9	2.3	54.0
	Dapsone, CTX	1	.5	1.1	55.2
	Enalapril	1	.5	1.1	56.3
	Fefol	1	.5	1.1	57.5
	Folic Acid	1	.5	1.1	58.6
	Haldol	1	.5	1.1	59.8
	HCTZ	3	1.4	3.4	63.2
	Hyoscine	2	.9	2.3	65.5
	KM	1	.5	1.1	66.7
	KM/LFX/PTO/CS/Pas	1	.5	1.1	67.8
	LFX/PTO/CS/PAS	1	.5	1.1	69.0
	NVP	1	.5	1.1	70.1
	Phenobarb	1	.5	1.1	71.3
	Predonolone	1	.5	1.1	72.4
	Pyrazinamide	1	.5	1.1	73.6
	Pyridoxine	1	.5	1.1	74.7
	RHZE	1	.5	1.1	75.9
	Spironalactone	2	.9	2.3	77.0
	TDF	1	.5	1.1	79.3
	TDF/3TC/EFV	6	2.8	6.9	86.2
	TDF/3TC/NVP	1	.5	1.1	87.4
	Vitamin B6	1	.5	1.1	88.5
	Z/BDQ/LFX/TRD	1	.5	1.1	89.7
	Z/KM/LFX/PTO/CS/PAS	1	.5	1.1	90.8
	Z/LFX/CS/PAS	1	.5	1.1	92.0
	Z/LFX/CS/PTO	1	.5	1.1	93.1
	Z/LFX/CS/PTO/PAS	1	.5	1.1	94.3
	Z/LFX/PTO/CS/PAS	2	.9	2.3	96.6
	Z/LFX/PTO/CS/PAS	1	.5	1.1	97.7
	Z/PTO/CS/LFX/R	1	.5	1.1	98.9
	Z/PTO/PAS	1	.5	1.1	100.0
	Total	87	40.3	100.0	
Missing		129	59.7		
Total		216	100.0		
Name of concomitant medicine-2					
Valid	Allopurinol	1	.5	3.7	3.7
	Atenolol	1	.5	3.7	7.4
	AZT/3TC/NVP	1	.5	3.7	11.1
	CTX	7	3.2	25.9	37.0

	Suspected medicine	Frequency	Percentage	Valid Percentage	Cumulative Percentage
	Dapsone, Flucon	1	.5	3.7	40.7
	Enalapril	1	.5	3.7	44.4
	Folate	1	.5	3.7	48.1
	Frusemide	1	.5	3.7	51.9
	Ibrufen	1	.5	3.7	55.6
	INH,CTX	1	.5	3.7	59.3
	Isoniazid	2	.9	7.4	66.7
	Ketoconazole	1	.5	3.7	70.4
	Methylopa	1	.5	3.7	74.1
	ORS	2	.9	7.4	81.5
	RHZE	1	.5	3.7	85.2
	TDF/3TC	1	.5	3.7	88.9
	TDF/3TC/EFV	3	1.4	11.1	100.0
	Total	27	12.5	100.0	
Missing		189	87.5		
Total		216	100.0		
Route of administration					
Valid	IM	13	6.0	6.4	6.4
	Oral	190	88.0	93.6	100.0
	Total	203	94.0	100.0	
Missing		13	6.0		
Total		216	100.0		
Indication for use of suspected medicine					
Valid	ADHD	1	.5	.5	.5
	ART	110	50.9	54.2	54.7
	Epilepsy	7	3.2	3.4	58.1
	Gastritis	1	.5	.5	58.6
	Hypertension	19	8.8	9.4	68.0
	IPT	4	1.9	2.0	70.0
	MDR-TB	17	7.9	8.4	78.3
	Measles	1	.5	.5	78.8
	Mood stabilizer	1	.5	.5	79.3
	Osteoarthritis	1	.5	.5	79.8
	Pain	2	.9	1.0	80.8
	Prevention of malaria	19	8.8	9.4	90.1
	Prophylaxis	12	5.6	5.9	96.1
	PTB	4	1.9	2.0	98.0
	Rud reactive	1	.5	.5	98.5
	Severe knee pain	1	.5	.5	99.0
	XDR-TB	2	.9	1.0	100.0
	Total	203	94.0	100.0	
Missing		13	6.0		
Total		216	100.0		
First reported ADR					
Valid	Abdominal discomfort	1	.5	.5	.5
	Abdominal pain	8	3.7	3.7	4.2
	Allergic reaction	1	.5	.5	4.6
	Anemia	11	5.1	5.1	9.7
	Angioedema	8	3.7	3.7	13.4
	Arthralgia	7	3.2	3.2	16.7
	Burning sensation of hands and feet	1	.5	.5	17.1
	Chest tightness	1	.5	.5	17.6
	Chills	1	.5	.5	18.1
	Confusion	1	.5	.5	18.5

	Suspected medicine	Frequency	Percentage	Valid Percentage	Cumulative Percentage
	Cough	13	6.0	6.0	24.5
	Cramps	1	.5	.5	25.0
	Depression	1	.5	.5	25.5
	Diarrhea	1	.5	.5	25.9
	Dizziness	6	2.8	2.8	28.7
	Dry mouth	1	.5	.5	29.2
	Foggy vision	1	.5	.5	29.6
	Gynecomastia	33	15.3	15.3	44.9
	Hallucination	1	.5	.5	45.4
	Headache	3	1.4	1.4	46.8
	Hearing loss	4	1.9	1.9	48.6
	Hepatitis	1	.5	.5	49.1
	Hypersensitivity reaction	1	.5	.5	49.5
	Hypokalemia	2	.9	.9	50.5
	Hypothyroidism	2	.9	.9	51.4
	Immunological failure	7	3.2	3.2	54.6
	Itching	3	1.4	1.4	56.0
	Jaundice	4	1.9	1.9	57.9
	Lipodystrophy	10	4.6	4.6	62.5
	Loss of energy	1	.5	.5	63.0
	Lymphadenopathy	1	.5	.5	63.4
	Malaise	2	.9	.9	64.4
	Nausea	3	1.4	1.4	65.7
	Pain	1	.5	.5	66.2
	Palpitation	1	.5	.5	66.7
	Pancytopenia	1	.5	.5	67.1
	Peripheral neuropathy	5	2.3	2.3	69.4
	Poor appetite	1	.5	.5	69.9
	Psychosis	4	1.9	1.9	71.8
	Rashes	28	13.0	13.0	84.7
	Renal dysfunction	15	6.9	6.9	91.7
	Steven Johnson Syndrome	1	.5	.5	92.1
	Tinnitus	5	2.3	2.3	94.4
	Toxic epidermal necrolysis	2	.9	.9	95.4
	Treatment failure	3	1.4	1.4	96.8
	Tremors	1	.5	.5	97.2
	Twisting of neck	1	.5	.5	97.7
	Ulceration and blisters on lips and mouth	1	.5	.5	98.1
	Vomiting	2	.9	.9	99.1
	Weakness	1	.5	.5	99.5
	Yellow eyes	1	.5	.5	100.0
	Total	216	100.0	100.0	
Second reported ADR					
Valid	Rashes	1	.5	1.6	1.6
	Anemia	3	1.4	4.9	6.6
	Angioedema	2	.9	3.3	9.8
	Bad urine	1	.5	1.6	11.5
	Blisters on hands and feet	1	.5	1.6	13.1
	Blockage in throat	1	.5	1.6	14.8
	Body ache	2	.9	3.3	18.0
	Body Itching	1	.5	1.6	19.7
	Cough	1	.5	1.6	21.3
	Inflammation of skin	1	.5	1.6	23.0
	Diarrhea	1	.5	1.6	24.6

	Suspected medicine	Frequency	Percentage	Valid Percentage	Cumulative Percentage
	Difficulty seeing	1	.5	1.6	26.2
	Difficulty walking	1	.5	1.6	27.9
	Discharging eyes	1	.5	1.6	29.5
	Dizziness	2	.9	3.3	32.8
	Drooling of saliva	1	.5	1.6	34.4
	Fever and chills	1	.5	1.6	36.1
	Gynecomastia	1	.5	1.6	37.7
	Headache	4	1.9	6.6	44.3
	Hearing loss	1	.5	1.6	45.9
	High creatinine	1	.5	1.6	47.5
	Hypokalemia	1	.5	1.6	49.2
	Jaundice	1	.5	1.6	50.8
	Loss of appetite	1	.5	1.6	52.5
	Lower abdominal pain	1	.5	1.6	54.1
	Malaise	4	1.9	6.6	60.7
	Nausea	3	1.4	4.9	65.6
	Night sweats	1	.5	1.6	67.2
	Numbness	1	.5	1.6	68.9
	Oral sores	1	.5	1.6	70.5
	Pain	1	.5	1.6	72.1
	Palpitations and fast heart beat	1	.5	1.6	73.8
	Peripheral neuropathy	1	.5	1.6	75.4
	Persistent clinical condition	1	.5	1.6	77.0
	Rashes	1	.5	1.6	78.7
	Red eyes	2	.9	3.3	82.0
	Reduced strength	1	.5	1.6	83.6
	Shortness of breath	1	.5	1.6	85.2
	Swollen lips	2	.9	3.3	88.5
	Vomiting	3	1.4	4.9	95.1
	Weight loss	2	.9	3.3	98.4
	Total	59	27.3	100.0	
Missing		157	72.7		
Total		216	100.0		
Third reported ADR					
Valid	Anemia	1	.5	3.2	3.2
	Backache	1	.5	3.2	6.5
	Bad urine	1	.5	3.2	9.7
	Cough	2	.9	6.5	16.1
	Cramps	1	.5	3.2	19.4
	Dark urine	1	.5	3.2	22.6
	Difficulty to pass urine	1	.5	3.2	25.8
	Dizziness	2	.9	6.5	32.3
	Dyspnea	1	.5	3.2	35.5
	Erythema	1	.5	3.2	38.7
	Headache	1	.5	3.2	41.9
	Itching of the eyes	1	.5	3.2	45.2
	Joint tenderness	1	.5	3.2	48.4
	Lipodystrophy	1	.5	3.2	51.6
	Loss of body weight	1	.5	3.2	54.8
	Loss of strength	1	.5	3.2	58.1
	Low abdominal pain	1	.5	3.2	61.3
	Mental instability	1	.5	3.2	64.5
	Nephrotoxicity	1	.5	3.2	67.7
	Palpitation	1	.5	3.2	71.0

	Suspected medicine	Frequency	Percentage	Valid Percentage	Cumulative Percentage
	Pruritus	1	.5	3.2	74.2
	Sores in mouth	1	.5	3.2	77.4
	Talks nonsense	1	.5	3.2	80.6
	Tingling	1	.5	3.2	83.9
	Ulcers inside mouth	2	.9	6.5	90.3
	Vomiting	3	1.4	9.7	100.0
	Total	31	14.4	100.0	
Missing		185	85.6		
Total		216	100.0		
Fourth reported ADR					
Valid	Body tremor	1	.5	11.1	11.1
	Constipation	1	.5	11.1	22.2
	Headache	3	1.4	33.3	55.6
	High Bp	1	.5	11.1	66.7
	Jaundice	1	.5	11.1	77.8
	Renal dysfunction	1	.5	11.1	88.9
	Sweating and nausea	1	.5	11.1	100.0
	Total	9	4.2	100.0	
Missing		207	95.8		
Total		216	100.0		
Severity of ADR by local grading					
Valid	Hospitalized	24	11.1	12.8	12.8
	Life threatening	8	3.7	4.3	16.5
	Not hospitalized	156	72.2	83.0	98.9
	Total	188	87.0	100.0	100.0
Missing		28	13.0		
Total		216	100.0		
Category of ADR report					
Valid	Adverse event	33	15.3	17.7	17.7
	Product use error	1	.5	.5	18.3
	Suspected major	11	5.1	5.9	24.2
	Suspected minor	141	65.3	75.8	100.0
	Total	186	86.1	100.0	
Missing		30	13.9		
Total		216	100.0		
Outcome of ADR					
Valid	Died	3	1.4	2.5	2.5
	Not yet recovered	87	40.3	71.3	73.8
	Persistent disability	3	1.4	2.5	76.2
	Recovered	29	13.4	23.8	100.0
	Total	122	56.5	100.0	
Missing		94	43.5		
Total		216	100.0		
Cadre of ADR reporter					
	Doctor	104	48.1	49.5	49.5
	Nurse	41	19.0	19.5	69.0
	Pharm tech	45	20.8	21.4	90.5
	Pharmacist	20	9.3	9.5	100.0
	Total valid count	210	97.2	100.0	
	Missing	6	2.8		
	Total count	216	100.0		