Ministry of Health and Social Services

Namibia Medicines Regulatory Council

Therapeutic Information and Pharmacovigilance Centre (TIPC)

ANNUAL FEEDBACK REPORT

STATISTICS ON ADVERSE EVENTS (APRIL 2021 - MARCH 2022)

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DEFINITIONS

Pharmacovigilance: the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem.

Adverse event: any untoward medical occurrence that may present during treatment with a pharmaceutical product, but which does not necessarily have a causal relationship with the treatment.

Adverse event following immunization: any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.

Adverse drug reaction: a noxious and unintended response to a medicine that occurs at a dose normally used in humans for prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function; the term ADR should be reserved for harmful or seriously unpleasant effects that call for reduction in the dosage, a withdrawal of the medicine, and/or a forecast of hazard from future administration.

Causality assessment: the evaluation of the likelihood that a medicine was the causative agent of an observed adverse drug reaction.

ABBREVIATIONS

AE	Adverse Event
ADR	Adverse Drug Reaction
AEFI	Adverse Event Following Immunization
WHO	World Health Organization
PV	Pharmacovigilance

INTRODUCTION

The Namibia Medicines Regulatory Council (NMRC) as established by the Medicines and Related Substances Act (Act No. 13 of 2003) has the mandate to regulate medicines and related substances circulating on the Namibian market. This is to ensure that at authorization and throughout their market life, medicines continue to be safe, efficacious and of quality.

The Therapeutics Information and Pharmacovigilance Centre (TIPC), is the Council's administrative and technical arm that carries out the pharmacovigilance responsibility to ensure safe and rational use of medicines.

Pharmacovigilance focuses on investigating and monitoring AEs after use of medicinal products, including those of vaccines i.e. AEFIs. Post-marketing pharmacovigilance is crucial to monitor the rare events as well as long-term safety of drugs, particularly in specific populations and situations that are not usually included in pre-marketing studies. Underlying this is the significance of appropriately collecting and reporting safety data to provide information for clinical and regulatory decision-making. Pharmacovigilance is essential in ensuring that medicines continue to be safe for use.

Rational and safe use of medicines also includes detecting medication errors. A medication error is defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is under the control of the healthcare professional, patient, or consumer (N. M. Elden & A. Ismail, 2016). Medication errors may occur at any stage during the drug delivery process from prescription to drug administration. They are costly for patients and their families, hospitals and their medical staff, and insurance companies, and can lead to serious complications, such as prolonged hospitalization, poor outcomes, and reduced quality of life (F. M. Alshammari, et al., 2021). Thus, medication error reporting is important as it provides an opportunity to learn and improve systems in an effort to reduce medicine use errors.

The ADR and AEFI reports received by the TIPC are entered into the World Health Organization's global database (VigiBase) and analysed periodically to identify any safety signals. Namibia has entered a total of 2 831 AE reports into the database since 2009.

The TIPC wishes to share the ADR, AEFI and medication error reports received during the 2021/22 financial year.

Pharmacovigilance is essential in ensuring that medicines continue to be safe for use.

STATISTICS

Reports by period

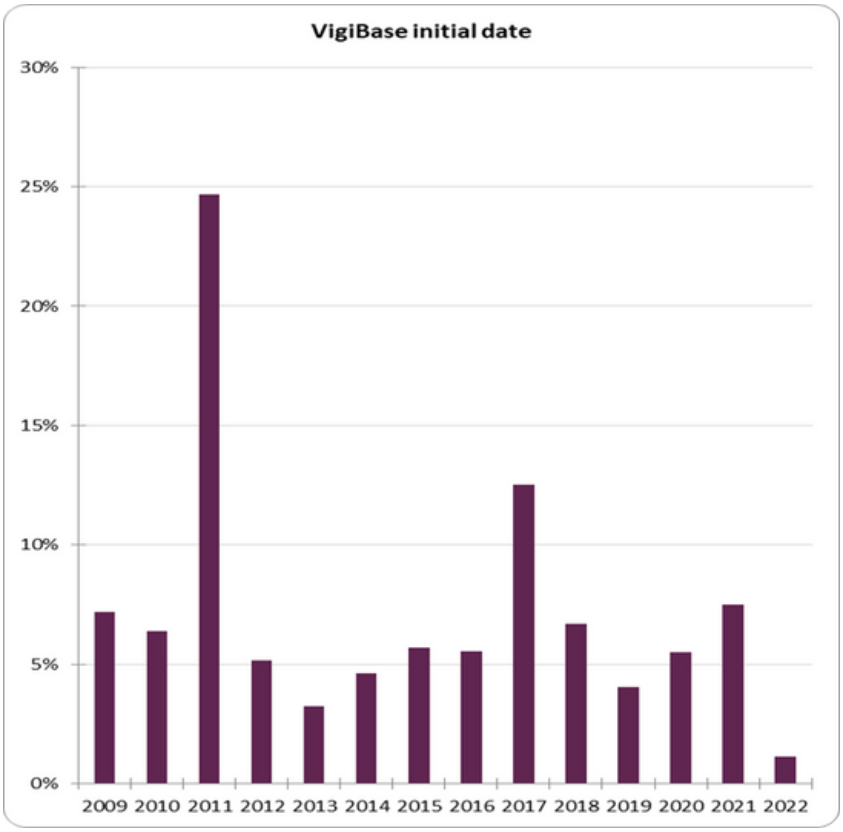


Figure 1: Percentage of AE reports in the WHO's global database (VigiBase) since 2009

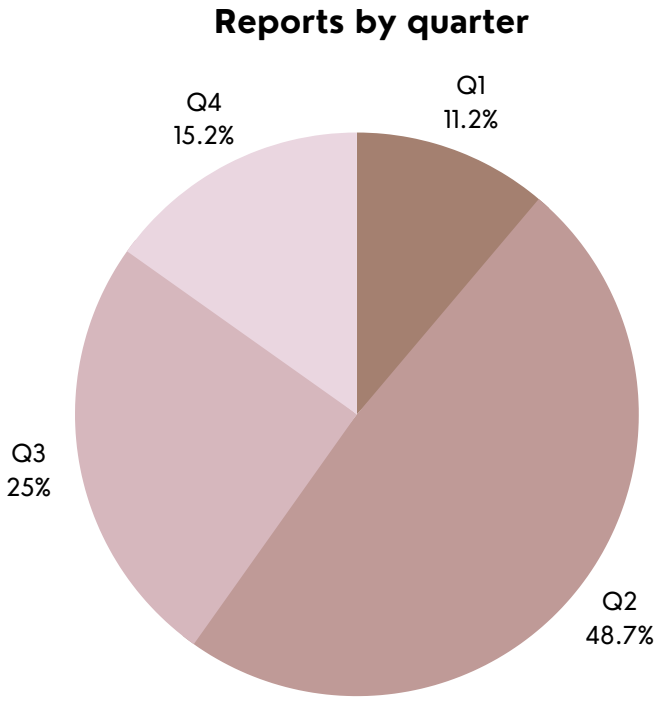


Figure 2: A total of 224 AEs reported from quarter 1 (April 2021) to quarter 4 (March 2022)

Reports by demographic information

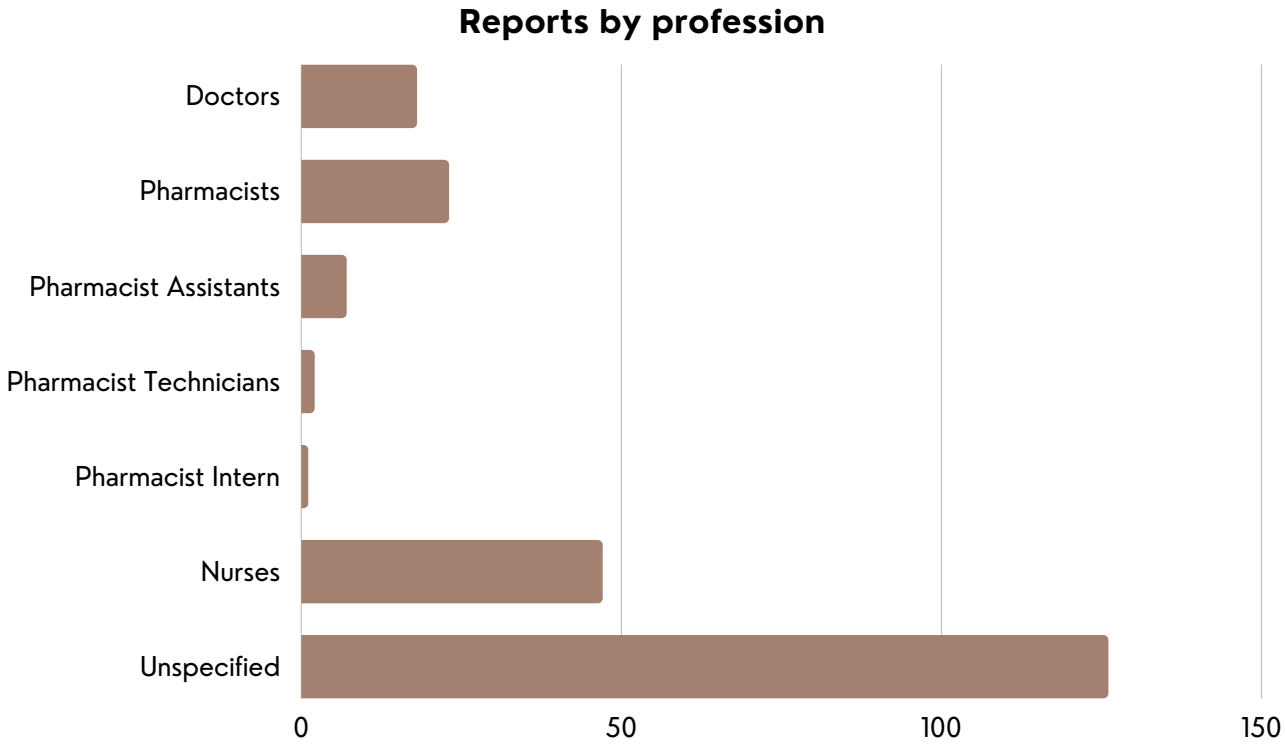


Figure 3: Number of reports received by profession

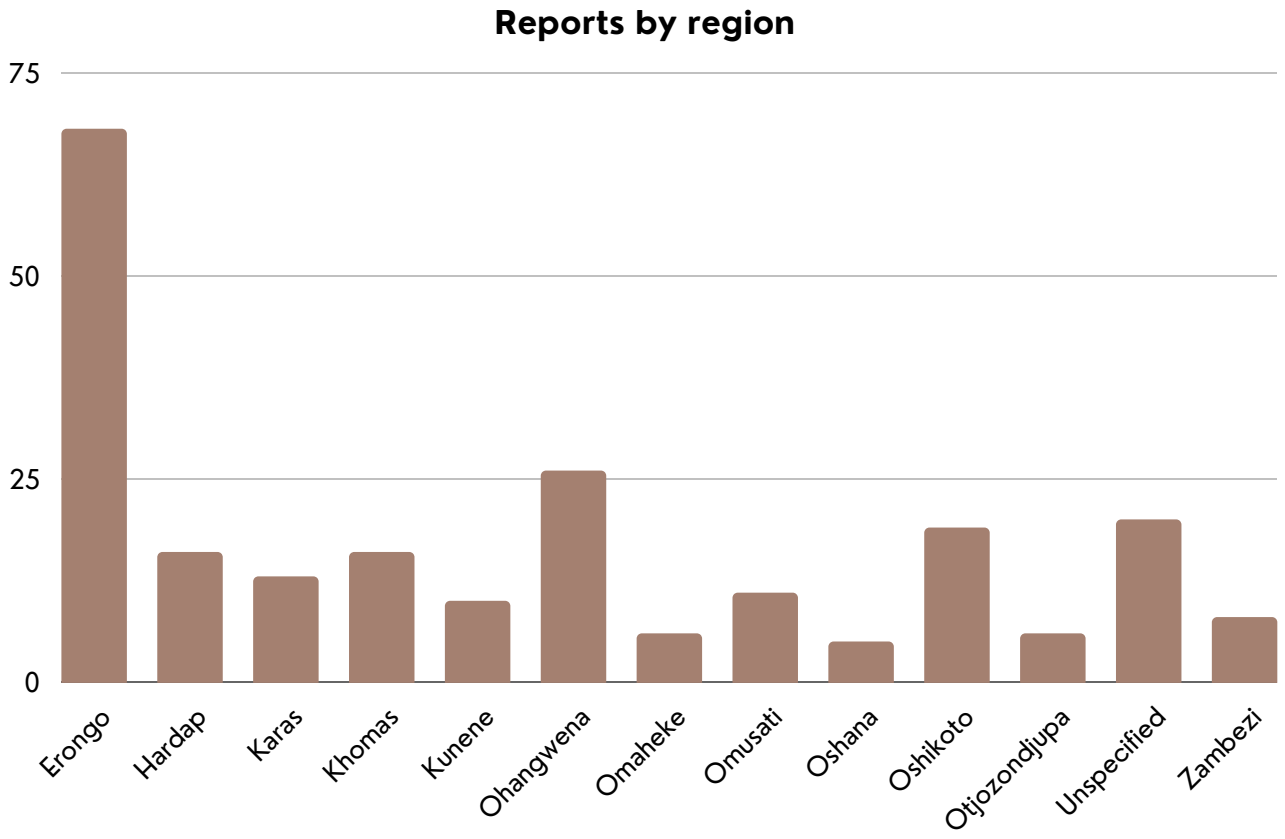


Figure 4: Number of reports received by region

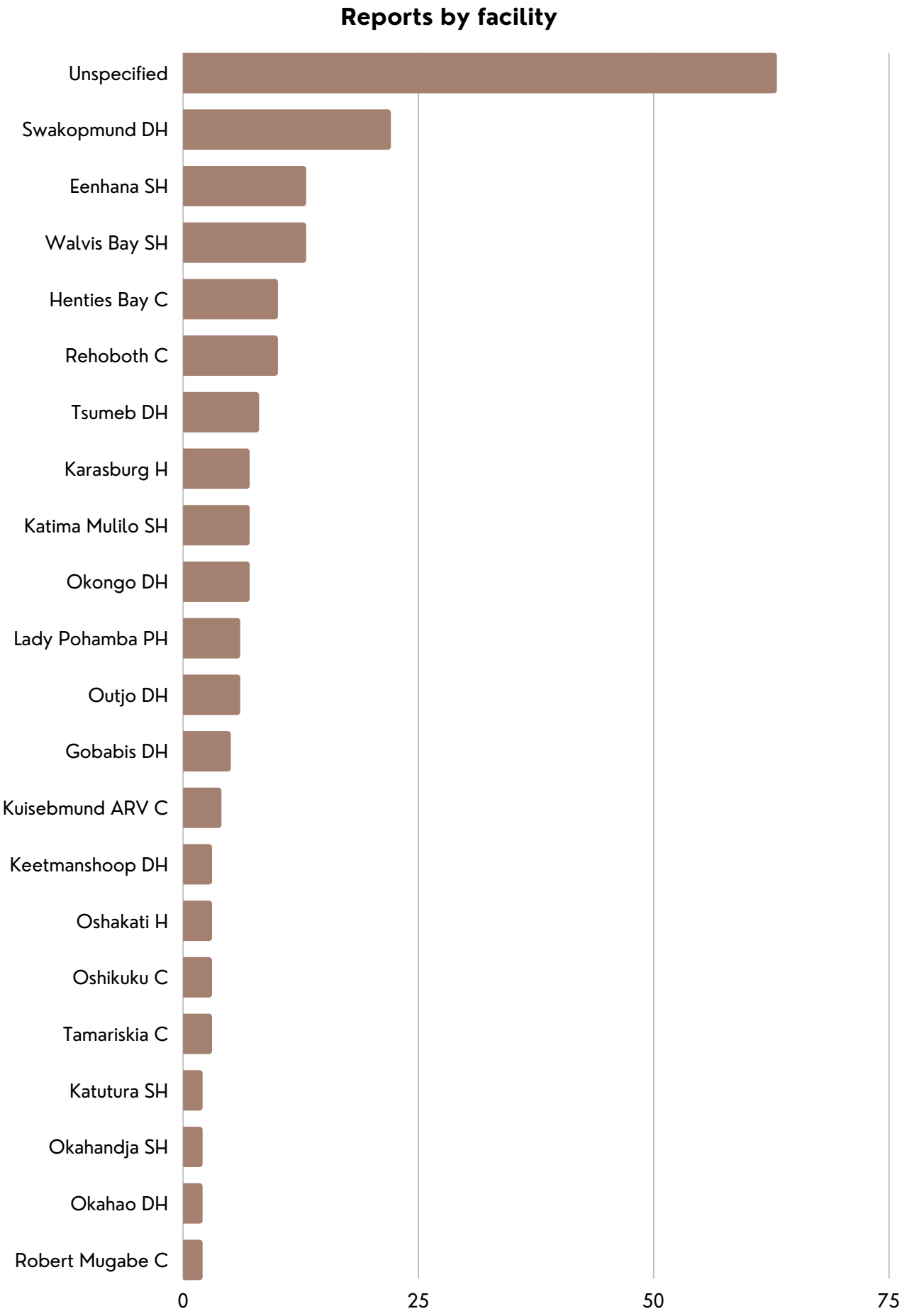


Figure 5: Number of reports received by healthcare facility

Overall reports

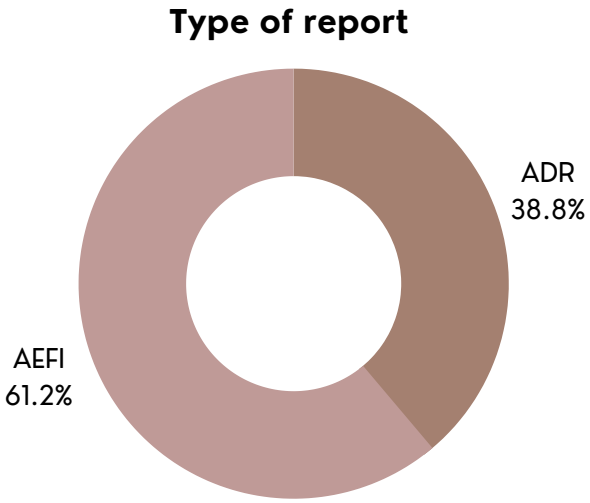


Figure 6: 87 ADRs and 137 AEFIs reported from quarter 1 (April 2021) to quarter 4 (March 2022)

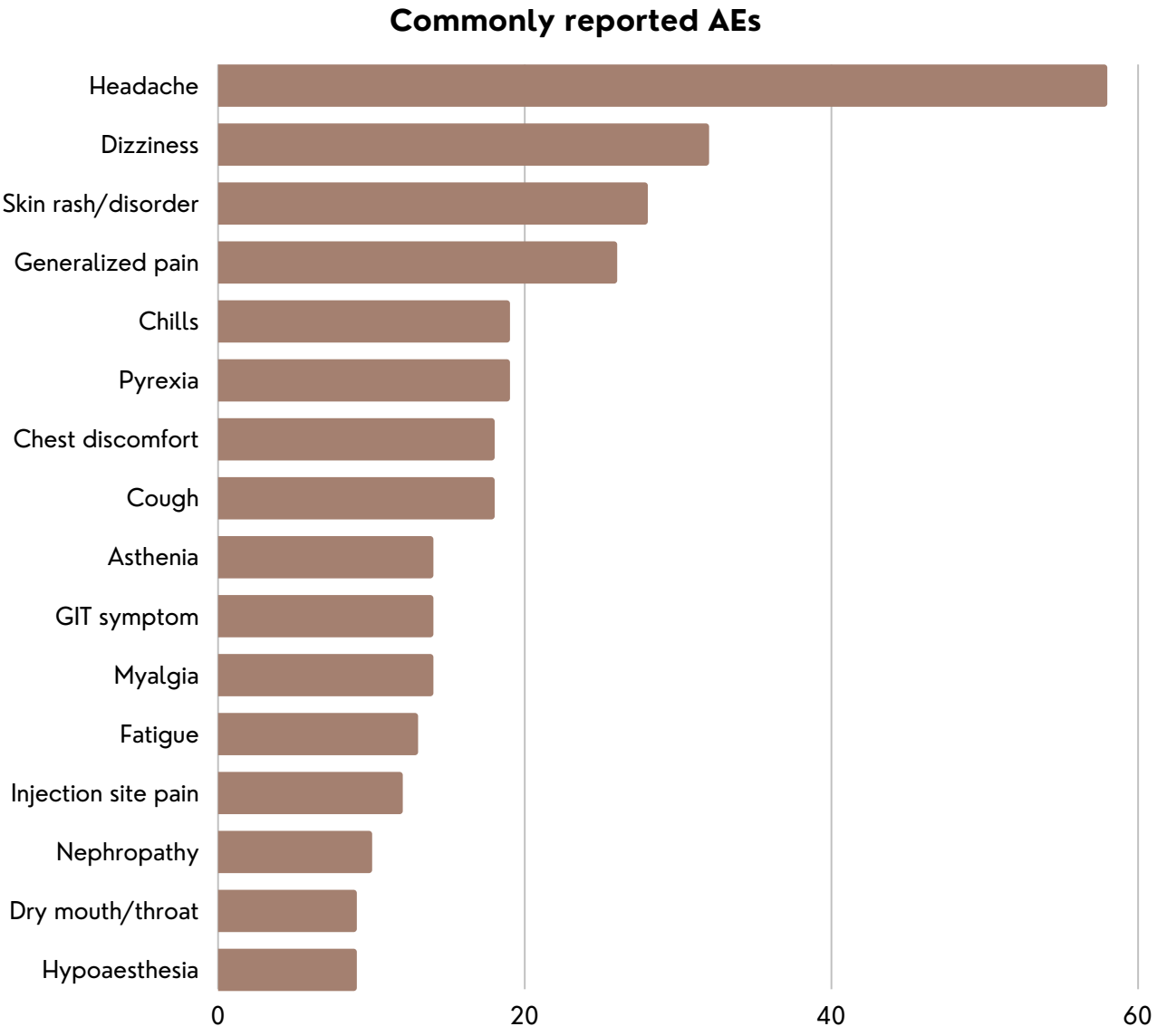


Figure 7: Common AEs reported

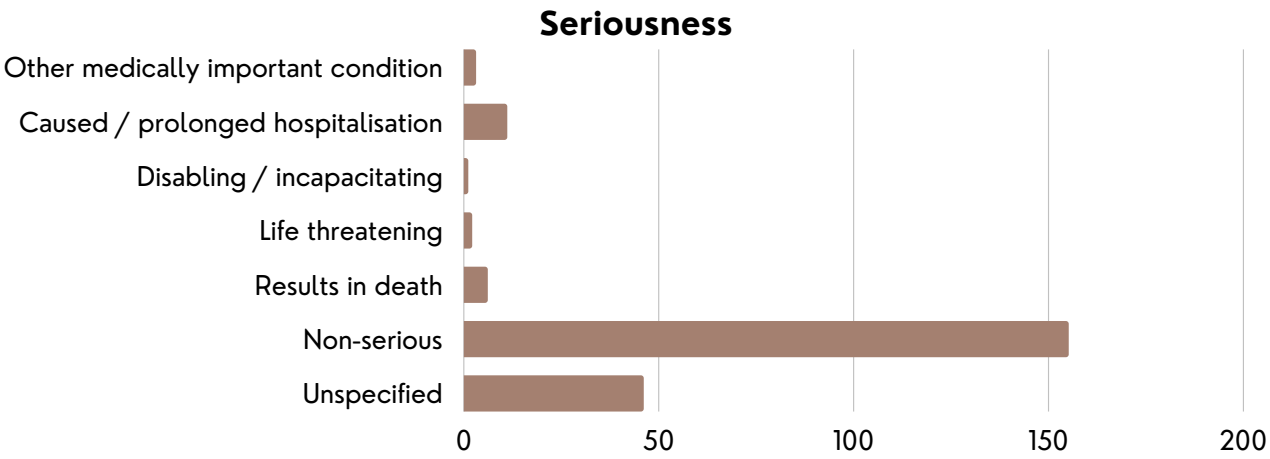


Figure 8: Seriousness of reported AE

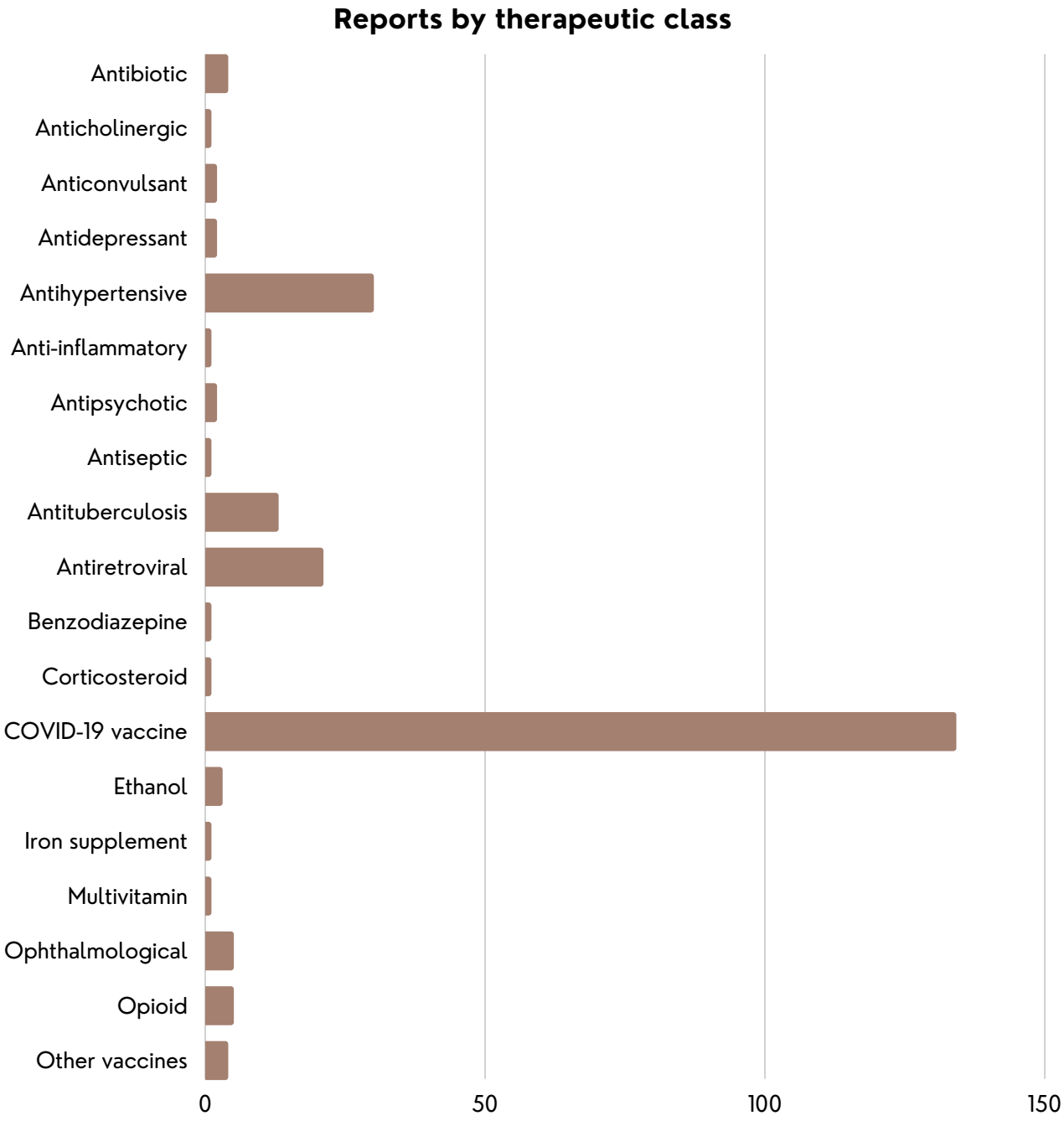


Figure 9: Number of reports by therapeutic class

Top reported therapeutic classes: COVID-19 vaccines & Antihypertensives

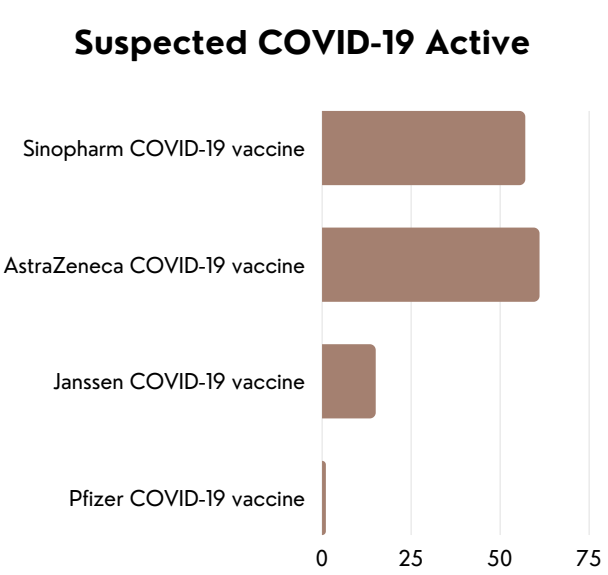


Figure 10: Number of reports received on COVID-19 vaccines

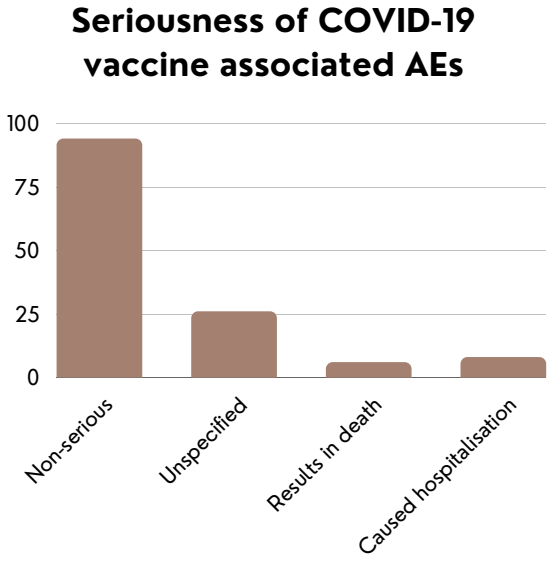


Figure 11: Seriousness of reported AEs associated with COVID-19 vaccines

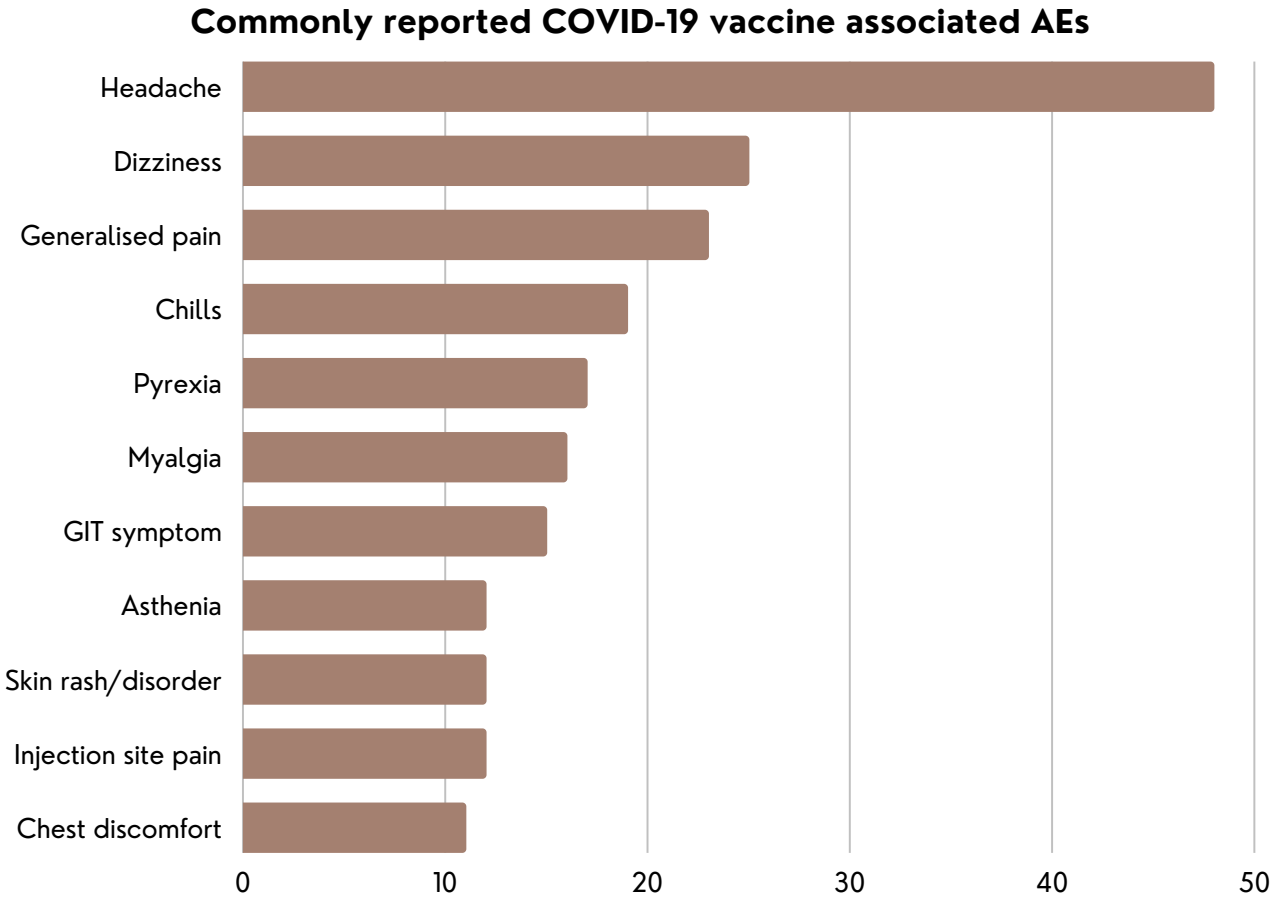


Figure 12: Commonly reported AEs associated with COVID-19 vaccines

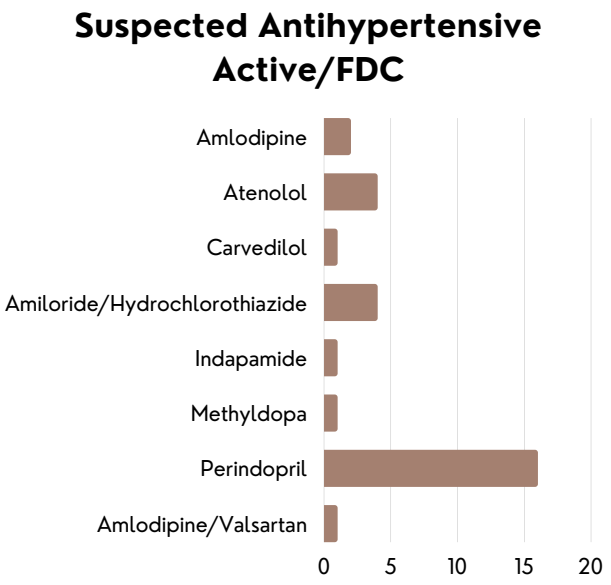


Figure 13: Number of reports received on antihypertensive drugs and Fixed Dose Combinations (FDC)

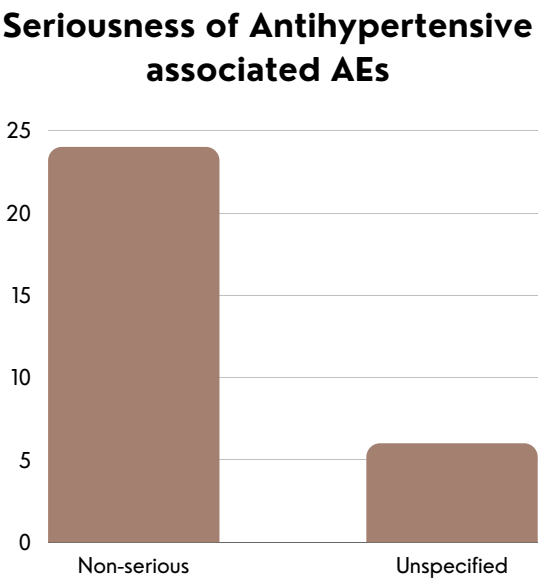


Figure 14: Seriousness of reported AEs associated with antihypertensive drugs

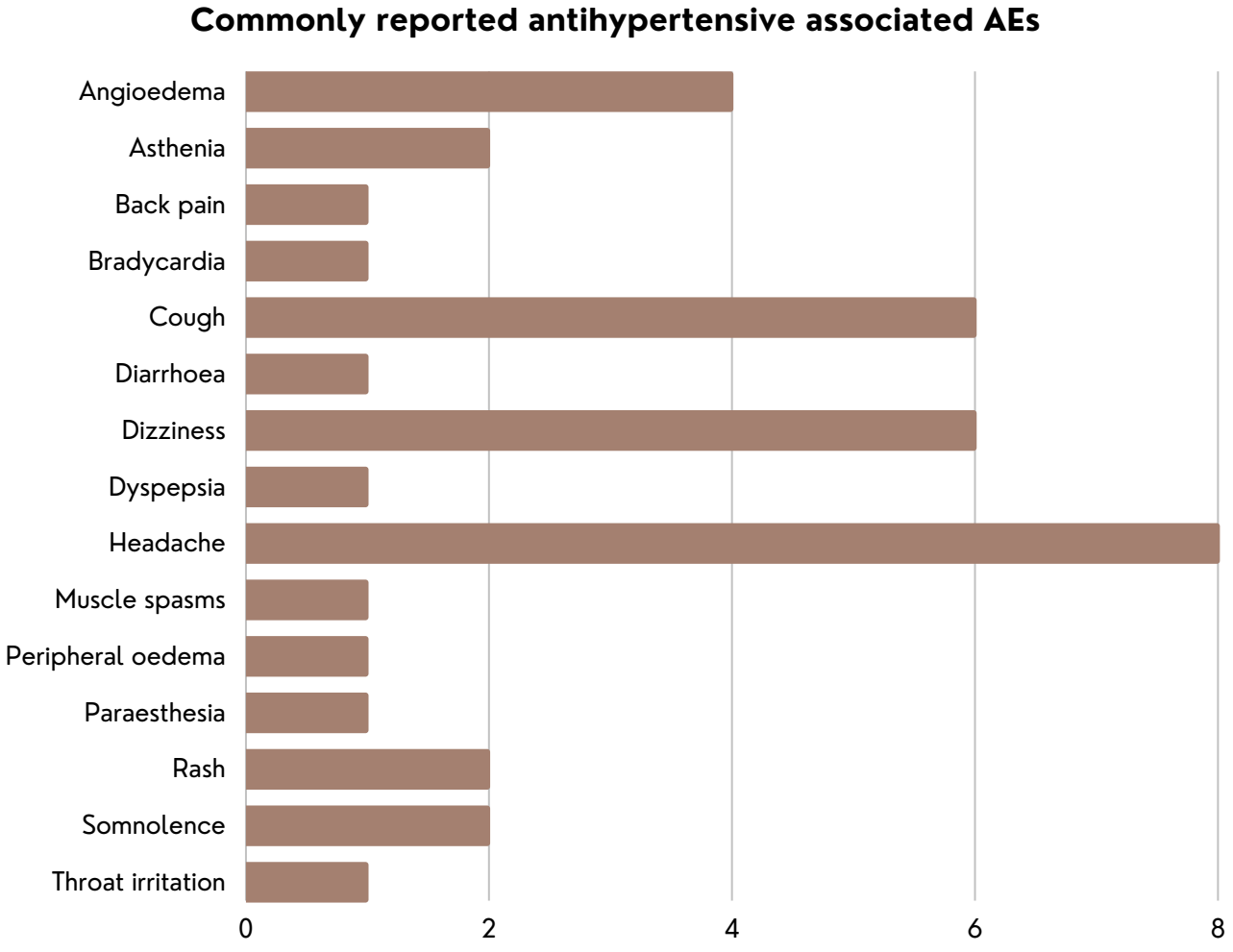


Figure 15: Commonly reported AEs associated with antihypertensive drugs

SUMMARY OF AE REPORTS

Reporter information

A total of 224 AE reports were received during the last financial year, with the highest number of reports recorded in the second quarter (Fig. 2). Compared to the previous financial year in which 117 AE reports were received, there has been an increase in the number of reports received. This is mainly attributed to the AEFI reports received after the introduction of COVID-19 vaccines. The bulk of the reports did not specify which health professional was reporting, therefore the nurses reported the most followed by pharmacists and then doctors (Fig. 3). A small proportion of reports was received through the e-Reporting tool.

The reports came from twelve (12) out of the fourteen (14) regions in Namibia with the leading regions being Erongo, Ohangwena and Oshikoto (Fig. 4). An analysis of the reporting facilities indicated that Swakopmund District Hospital submitted the most reports, followed by Eenhana Hospital, Walvis Bay Hospital, Rehoboth Clinic and Henties Bay Clinic (Fig. 5). Overall the AEFI reports were 137, whilst the ADR reports were 87 (Fig. 6).

Adverse event information

Headaches, dizziness, skin rash/disorders, generalized pain and chills comprised the frequently reported AEs (Fig. 7).

The majority of reports received were categorized as non-serious (69%). Some of the reported AEs resulted in prolonged hospitalization (5%), a few resulted in death (3%), very little were reported to have caused other medically important conditions, a small number were reported to be life threatening and a much smaller number were reported to be disabling/incapacitating (Fig. 8).

There were a few adverse events considered to be serious by the reporters. Some of the adverse events, according to literature, may be due to the suspected drug as reported by the reporter. However, simultaneously there are also some adverse events that were not documented in literature as associated with the suspected drug as reported by reporter and therefore may not be due to that particular drug.

The COVID-19 vaccines and antihypertensive medicines were the top therapeutic classes suspected to cause a high number of the AEs (Fig. 9). AstraZeneca's COVID-19 vaccine (45.5%) was most reported to cause AEs followed by Sinopharm COVID-19 vaccine, Janssen COVID-19 vaccine and then Pfizer COVID-19 vaccine (Fig. 10). The majority of the AEs suspected with the COVID-19 vaccines were non-serious (70%) a few resulted in prolonged hospitalization (6%) and a small number resulted in death (4%) (Fig.11). All the COVID-19 vaccines had several reports indicating headache as an adverse event, which explains headache as being the most reported AE. Headache is an expected and common AEFI for all COVID-19 vaccines (Fig.12).

Investigations were carried out for the serious AEFIs. Following the investigations, the National AEFI Committee assessed causality according to the WHO AEFI causality assessment tool. A detailed report on all the AEFIs, including AEFIs with death as an outcome, will be issued in the **AEFI Surveillance Report April 2021 – March 2022** by the Ministry of Health and Social Services.

The most reported antihypertensives were perindopril (53.3%) followed by amiloride/hydrochlorothiazide and atenolol (Fig. 13). The majority of the AEs suspected with antihypertensives were non-serious (80%), and the seriousness of the rest of the AEs related to antihypertensives were not specified in the reports (Fig. 14). Headache, followed by dizziness and cough were commonly reported with the antihypertensives. The frequently reported cough was mainly suspected with perindopril, the headache and dizziness was mostly suspected with perindopril and amiloride/hydrochlorothiazide (Fig. 15).

ADDITIONAL INFORMATION

Vancomycin and Red man syndrome

Although not highly reported to TIPC, red man syndrome is a common allergic reaction to vancomycin. Red man syndrome is an infusion-related reaction particular to vancomycin. It usually consists of pruritus that involves the face, neck and upper torso. Less often, hypotension and angioedema may occur. Patients usually complain of diffuse burning and itching and of generalized discomfort (S. Sivagnanam & D. Deleu, 2003).

Signs and symptoms of red man syndrome appear about 4 – 10 minutes after an infusion started or may begin soon after its completion. It is oftentimes associated with rapid (< 1 hour) infusion of the first dose of vancomycin (S. Sivagnanam & D. Deleu, 2003).

Red man syndrome, which is an anaphylactoid reaction, is caused by the degranulation of mast cells and basophils, leading to the release of histamine independent of preformed IgE or complement. The extent of histamine release is partially related to the amount and rate of the vancomycin infusion. The effects of red man syndrome can be relieved by antihistamines. Administration of diphenhydramine to patients prior to starting vancomycin infusion can prevent the occurrence of red man syndrome with the first dose of vancomycin (S. Sivagnanam & D. Deleu, 2003).

In short, each intravenous dose of vancomycin should be administered over at least a 60-minute interval to minimize the infusion-related adverse effects. Longer infusion times should be used in patients receiving doses considerably larger than 1g of vancomycin.

Rifapentine associated adverse events

Rifapentine was introduced in Namibia in August 2020, and is therefore a fairly new drug on the Namibian market. It belongs to a class of drugs called rifamycins and is the cornerstone of newer short-course TB prevention therapy (TPT). When combined with a second TB drug, isoniazid, rifapentine forms the 3HP regimen which is taken once weekly for 12 weeks. The 3HP provides a shorter alternative to the older standard of care, called isoniazid preventive therapy (IPT), in which people take isoniazid every day for between six and 36 months (M. Frick, 2020).

Rare adverse events called hypersensitivity reactions have been reported in both clinical trials and programmatic use of rifapentine. These reactions are frequently characterized by flu-like symptoms. Hypersensitivity episodes are uncommon and usually resolve swiftly after medication is stopped without any long-term effects. The cause of these reactions is unknown as they could be due to rifapentine, isoniazid, or the combination of the two (M. Frick, 2020).

MEDICATION ERROR REPORTS

In the 2021/22 financial year, a total of three (3) medication error reports were received. Two (2) reports involved incorrect dose administration and one (1) incorrect time of administration.

The two (2) incidents of incorrect dose administration were due to the infusion set not completely closed and not using a buretrol during medication administration. The one (1) incident of incorrect time of administration occurred when a healthcare professional wrongfully immunized a two-week-old infant with Polio, Pneumococcal, Pentavalent and Rotavirus vaccines. The infant's age was only confirmed post-immunization by verifying the date of birth in the health passport after observing that the infant appeared rather small. The correct age for this immunization is six-weeks.

Medication errors are a reality that will inevitably occur, as medical personnel and patients are human and, therefore, susceptible to error. Errors are generally multifaceted and can occur at any point within the complex process of medication administration.

The most important knowledge in the field of patient safety is how to prevent harm to patients during treatment and care. The fundamental role of a patient safety reporting system is to enhance patient safety by learning from failures of the health-care system. Health-care errors are often exacerbated by weak systems and often have common root causes which can be generalized and corrected. Although each event is unique, there are likely to be similarities and patterns in sources of risk which may otherwise go unnoticed if incidents are not reported and analyzed.

Errors may never be entirely eliminated, but strategies can be put in place to minimize the probability of errors occurring. Healthcare workers are encouraged to identify and respond to signs that an error in prescribing, calculation or administration may have occurred, so that harm can be prevented or reduced.

One method of preventing medication errors is ensuring a workforce of highly skilled healthcare professionals who are able to meet the demands of complex schedules. This further highlights that continuing professional development (CPD) is essential for healthcare professionals to maintain and acquire the necessary knowledge and skills to provide person-centred, safe and effective care. Therefore, efforts to reduce medication errors should focus on these human factors.

Without medication error reporting, opportunities for learning are diminished. It is therefore important to recognize and report medication errors, as this will help learn from them as well as prevent them in the future.

SHORTCOMINGS

Low reporting

Although the total number of reports in the past financial year has increased when compared to the previous year, this is mainly due to the AEFI reports received as a result of the COVID-19 pandemic and the rollout of the COVID-19 vaccines. A decline in the number of ADR reports received has been observed in the past financial year. According to WHO recommendations, with a population of 2.6 million Namibia is expected to report at least 520 AE reports per reporting year. However, TIPC has recorded less than 50% of the expected AEs, indicating under-reporting.

Missing information

A number of ADR and AEFI reports are missing critical information such as drug name, date drug started, adverse event and date adverse event started. This poses a great challenge especially when assessing causality of the case reports.

In addition, there is a number of reports were the region and/or healthcare facility were not indicated. Hence the unspecified regions and healthcare facilities observed in the graphs.

Reporter information such as email address and contact number were also missing in some reports, making it extremely difficult for the TIPC team to follow up on reported information when required as well as provide the necessary feedback to the reporters.

All healthcare professionals are therefore encouraged to extensively complete the ADR and AEFI reporting forms. In addition, healthcare professionals such as pharmacy staff who coordinate pharmacovigilance activities in their facilities should verify completion of the reports before sending them to the TIPC.

ACTIVITY PLANS

1

Active Surveillance Training

The TIPC in collaboration with partners is planning a face-to-face training for the implementation of active surveillance and active drug safety monitoring for HIV and TB medicines, which will allow for the active monitoring of AEs in the two programmes.

2

ADR Monitoring Survey

The TIPC will be sharing a survey on ADR monitoring with stakeholders. The aim of the survey is to recommend approaches to improve the services provided by TIPC.

3

MedSafetyWeek Campaign

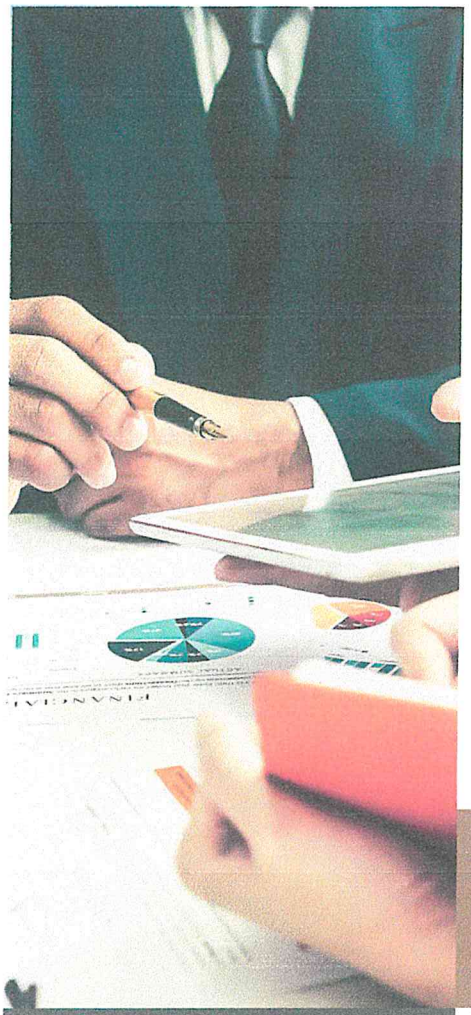
#MedSafetyWeek is an annual social media campaign dedicated to creating awareness on pharmacovigilance. In 2021, #MedSafetyWeek took place during the week of 1-7 November and the theme was birthed by the COVID-19 pandemic and ultimately centered on vaccines safety, particularly encouraging the reporting of suspected side effects following vaccinations.

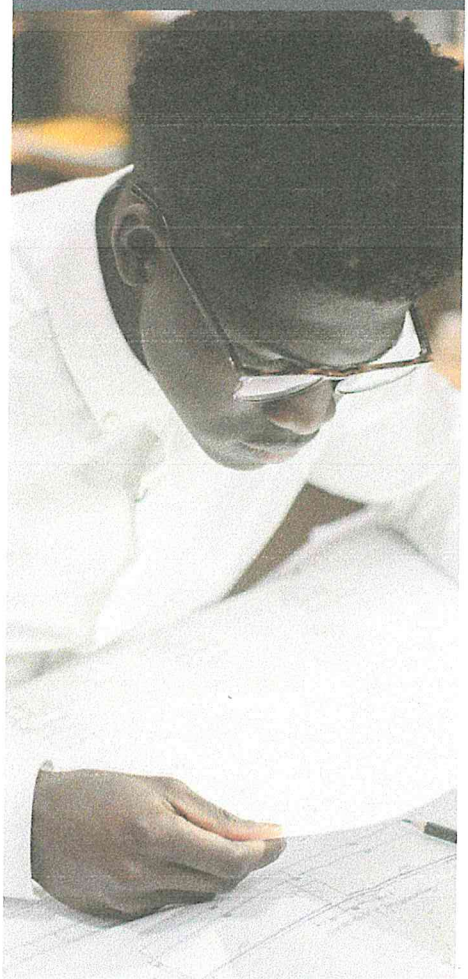
More information regarding this year's MedSafetyWeek Campaign will be shared in due course.

4

Strengthening Pharmacovigilance and Regulatory Capacities in four Southern African Countries (SPaRCS)

The TIPC initiated joined activities of the SPaRCS project funded by the European and Developing Countries Clinical Trials Partnership (EDCTP). The aim of SPaRCS is to strengthen pharmacovigilance (PV) systems and clinical trials oversight of National Regulatory Authorities (NRAs) in Namibia, South Africa, Eswatini and Zimbabwe. One of the outcomes of SPaRCS is to incorporate community health workers (CHW) in PV. Further information regarding how and when CHW will be incorporated in PV will be shared by TIPC in due course.





ACKNOWLEDGEMENTS

The TIPC team wishes to thank all healthcare workers for their continuous dedication to the safety monitoring of medicines on the Namibian market by reporting suspected ADRs as well as AEFIs and most importantly ensuring that patients are appropriately managed.

Furthermore, the TIPC team also wishes to thank healthcare workers for reporting medication errors, as these provide opportunities to learn and improve systems.

Healthcare professionals can reach out to TIPC for technical support on pharmacovigilance.

CONTACT

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e-Reporting: **https://primaryreporting.who-umc.org/NA**

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