MODULE III

Learning how to report ADRs

This is a joined presentation between
NPC and SAHPRA

Presenter:
Mrs Victoria Sekiti
(Medicine Regulatory Officer)

30 November 2023
14h00 – 16h00

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

SAHPRA
South African
Health Products
Regulatory Authority

2030 NDP

Objectives

- Explain when to report an ADR
- Describe what would constitute a good ADR report
- Report an ADR

We will achieve these objectives by answering the 5 W's and 1H of reporting
- Why, What, When, Who, Where, and How

Objective 1

Explain when to report an ADR

Common reasons for not reporting

- Time-consuming
- Lack of feedback
- Not sure whether report is valid or useful
- Already known side effect of medicine
- No access to the form / don't know how, where, when to report etc.
- Legal liabilities if there was a medication error
- Insufficient clinical or pharmacology knowledge
- Won't make a difference

In this module we will address these reasons!

Why the need to report ADRs?

- Information about the safety profile of a medicine at the time of marketing is limited.
- Therefore, we do know enough about:
  - How the medicine will perform in a much more varied population with other conditions and genetics.
  - Different ways in which the medicine will be used by people
  - Other medicines, foods and chemicals that may interact with the medicine.
  - Long term effects of the medicine.
  - How the medicine will perform in special populations not included in clinical trials.

What to report to SAHPRA?

All suspected ADRs

Do you suspect an ADR?

Yes

Is it serious? — Yes → Report ADR

No

Is it well described in the PI/PIL? — No → Report ADR

Yes

Is it a new product? — Yes → Report ADR

No

Is the patient part of a special population? — Yes → Report ADR

No

Not necessary to report ADR

When in doubt - REPORT!

Do you suspect a problem of product quality?

Yes

Did it result in an ADR? — Yes → Report ADR

No

Report as product quality problem in ADR form (retain sample)

When to report an ADR?

Ideally - as soon as the ADR is suspected, and you have at least the *minimum information*

Recommended Reporting Timelines:

- Serious cases – within **24 hours** of identification
- Non-serious cases - within **15 calendar** days of identification
- **Please report even if beyond this time frame!**

Report even when **all facts are unavailable**, or you are **not sure** that the medicine is responsible for the ADR.

The sooner we know about the problem, the less public health harm it is likely to cause!

Objective 2

Describe what would constitute a good ADR report

What constitutes a valid ADR report?

The minimum information for a valid report?

One Single Identifiable patient

Identifiable& **contactable** Reporter

One or more suspected ADR

One or more Suspected medicinal product

Remember: valid report ≠ complete report

Components of a good ADR report

Patient

- initials/folder #
- Age/DOB group
- Gender
  - Female Pregnancy
- Additional information -
- Other conditions, medicines and relevant medical history

Reporter

- Name
- Contact details
- Qualification
- Date of report

Suspected Medicine/s

- Brand/trade name
- Active ingredient/s
- Trade name & batch No. esp. for vaccines, biologicals & product quality issues
- Strength, dose, dosage form & frequency
- Route of administration
- Indication of use
- Duration of usage (start & end date).

Suspected Reaction

- Description of the ADR (All signs & symptoms)
- Timing of onset
- Confirmed diagnosis
- Relevant lab tests & results of investigations
- De-challenge and Re-challenge
- Seriousness of the reaction
- Expectedness
- Outcome of event (Rx used if any)

The Importance of Complete ADR Report

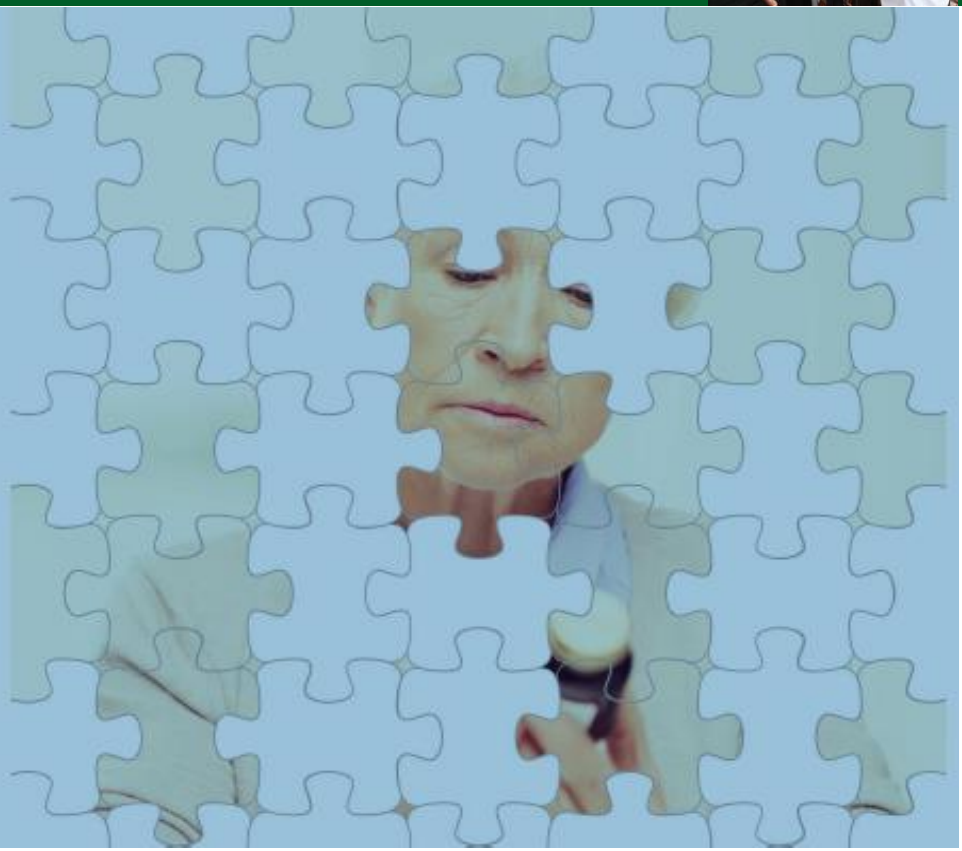
A woman

is treated with paracetamol.

She develops liver injury and breast cancer in 2013 .

No further information available.

Unclassifiable



The Importance of Complete ADR Report

A 14 yr old boy

Is treated with ibuprofen 400 mg twice daily after having sprained his left ankle.

On the second day of treatment he develops hives from head to foot, swollen lips, itching and collapses within 30 minutes of drug intake.

His blood pressure is 80/50 mmHg, his heart rate 144/minute.

He recovers promptly after emergency treatment with adrenalin and iv fluids.

He had been treated with ibuprofen several months before without any problem.

Dechallenge and Rechallenge

Rechallenge and Dechallenge information helps us understand whether the medicine/s caused the reaction.

Dechallenge = What happens when the suspected medicine is stopped

- Negative dechallenge = Event continues to occur after medicines is stopped.
- Positive dechallenge = Partial or complete removal of event after medicine is stopped.

Rechallenge = What happens when the suspected medicine is reintroduced in the patient after positive dechallenge

- Negative rechallenge = Event did not re-occur when the suspected medicine is restarted.
- Positive rechallenge = Reoccurrence of similar signs and symptoms when suspected medicine is restarted.

Why do we gather all this information?

This information helps us to answer the following questions:

- How sure are we that the suspected medicine did cause this suspected ADR? (Causality Assessment)
- Does this case contribute evidence that this reaction may occur in other patients exposed to this medicine? (Signal detection)
- Which patient groups may be at higher risk of such a reaction? (Risk factors)
- How exactly does such an adverse event present in a patient? (nature and severity of reaction)
- How do these suspected ADRs evolve and how are they managed? What treatments have been successful or not?

What if you receive additional information?

New information could include:

- Final outcome of the patient (may have recovered or deteriorated)
- Additional lab tests or results of investigations
- Additional dechallenge or rechallenge information
- Important other information that may contribute to ruling out other possible causes

In this case the reporter should report this follow-up information as **"follow up report"** and quote the unique reference number from the previous report generated by the online reporting portal.

Who can report an ADR?

Doctor (including specialists)
and Medical Assistants

Patients/ Caregivers

Nurse/Midwives
Nursing Assistants

Pharmacist and Assistants

Complementary and Traditional Practitioners

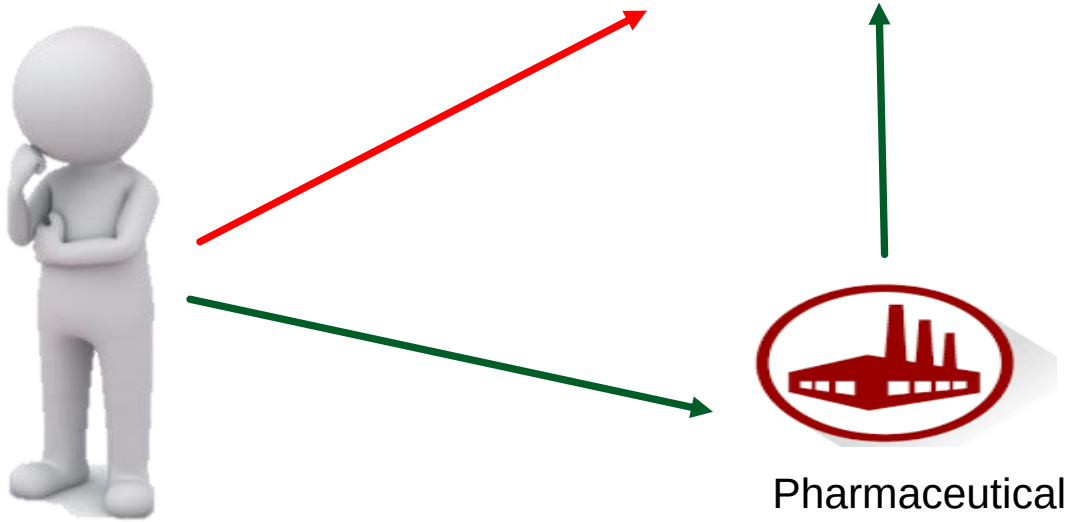
Paramedics

Dentists and other health professionals

Where to report an ADR?

Report to either

SAHPRA
South African Health Products Regulatory Authority



Pharmaceutical company relevant to the suspected drug

How to report an ADR?

Med Safety App

eReporting (link from SAHPRA website)

Adverse Drug Reactions & Quality Problem Reporting Form

Email – adr@sahpra.org.za

Objective 3

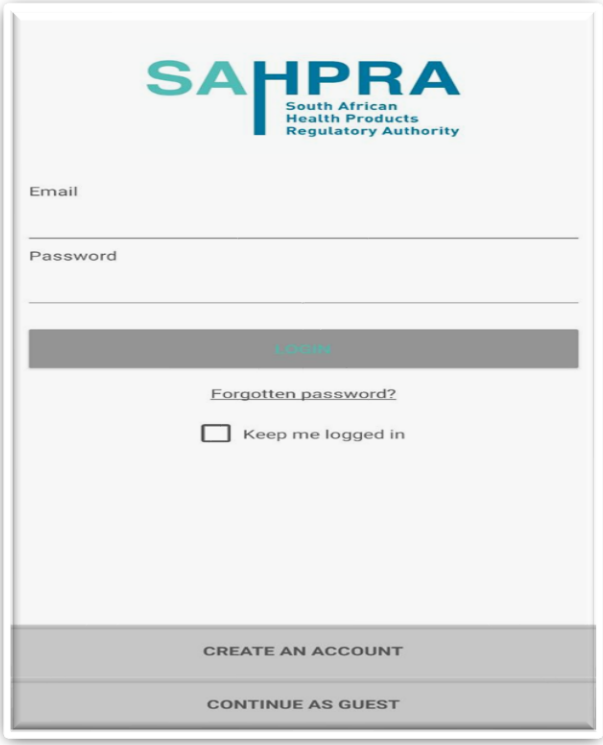
- Report an ADR

Med Safety App

The preferred tool for reporting suspected ADRs

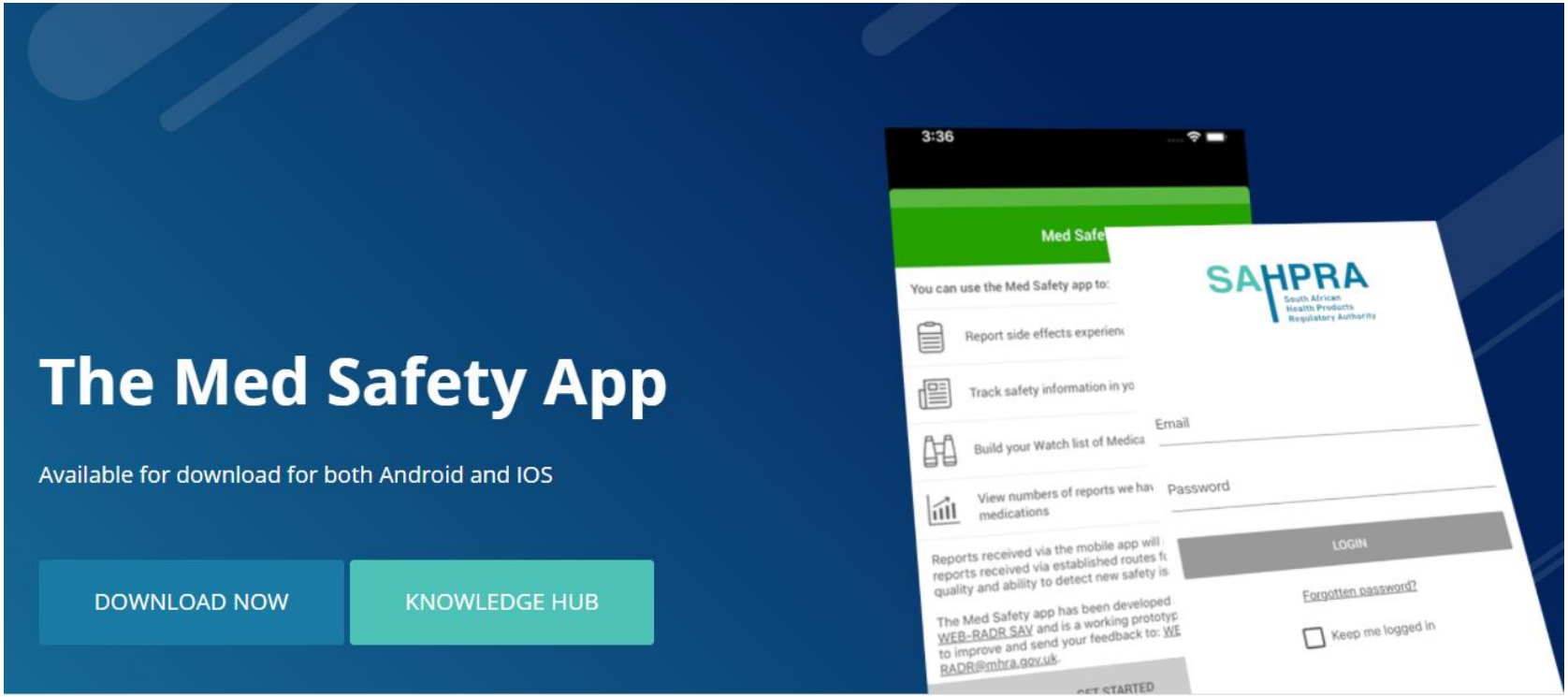
- How To Download The Med Safety App?

1. Open the Play Store (Android) or the App Store (IOS).
2. Search for Med Safety icon.
3. Tap the Med Safety icon to install to the download the App.
4. Tap Open.
5. Select a region “South Africa”, sometimes it selects automatically depending on the settings you already have on your phone.

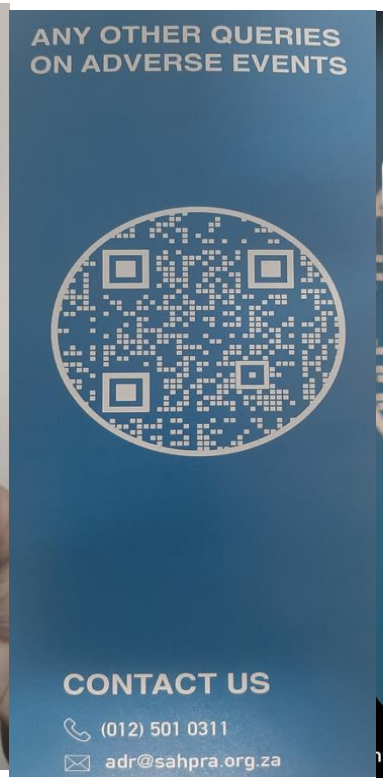


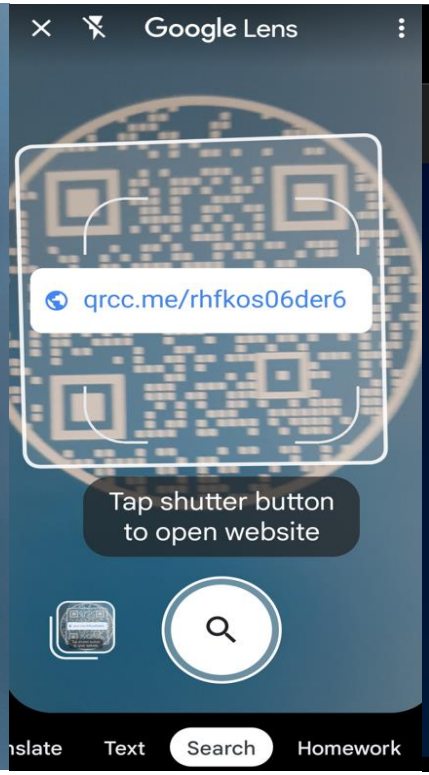
Med Safety App

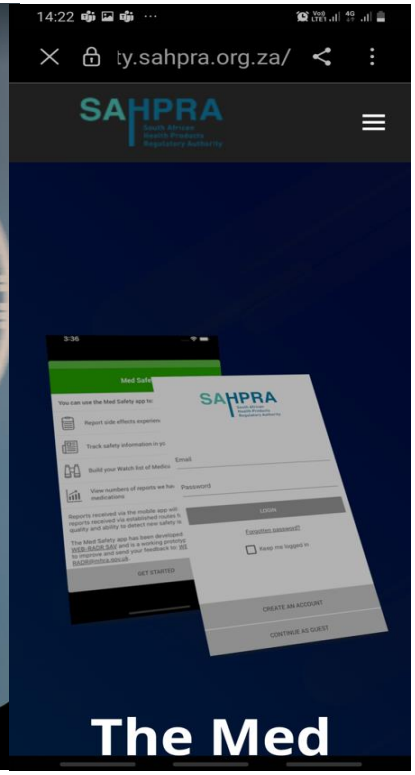
Access link: Medsafety X SAHPRA



Med Safety App - Brochure







Med Safety App

Med Safety App Navigation

https://youtu.be/jvuQZddyFTM

Med Safety App Ack Report

SAHPRA
South African Health Products Regulatory Authority

Dear Victoria Sekiti

Your report of a suspected side-effect of a medicine.

Registration Number: ZA-SAHPRA-2021021815593[redacted]

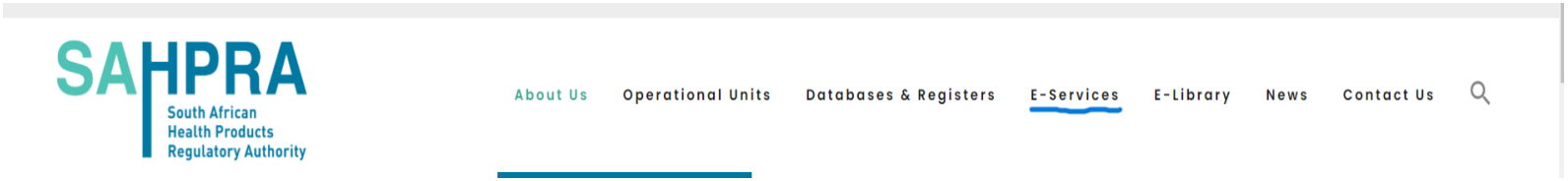
Thank you very much for completing a report on the suspected side-effect of a medicine. We really appreciate your contribution because every adverse drug reaction we receive helps us to monitor the safety of medicines.

Our staff analyse the database regularly to look at the relationship between medicines and side-effects. We receive thousands of reports every year, and when we spot a possible new link between a medicine and a side effect we quickly look into it to see if there is a problem. If there is, we consider whether the risk is common or serious, and decide if we need to do anything. For instance, we may add warnings to the leaflet that comes with the medicine. Or we may update information on how the medicine should be used - for instance, limiting the dosage, or saying that it should not be used by particular groups of patients. Rarely, we may take the medicine off the market, but only if we consider that the risks of the medicine outweigh its benefits.

Due to the number of reports we receive, we cannot write to everyone with details

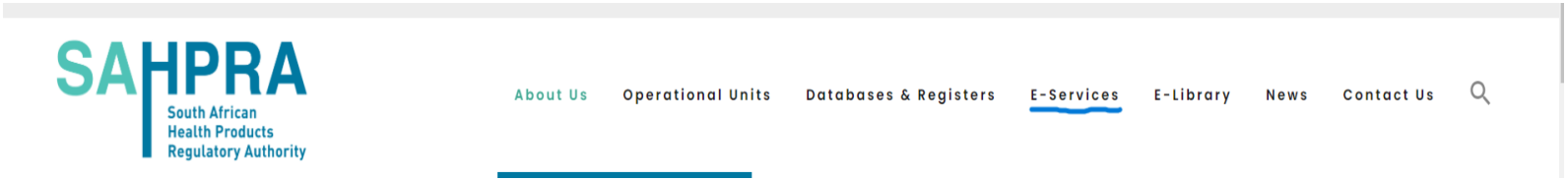
e-Reporting Portal

Access link: https://www.sahpra.org.za



e-Reporting Portal

Access link: https://www.sahpra.org.za



Navigation of e-Reporting Portal

Access link: https://www.sahpra.org.za

Navigation of e-Reporting Portal

Access link: https://www.sahpra.org.za

SAHPRA
South African
Health Products
Regulatory Authority

Adverse drug reaction and product quality reporting

Here you can report adverse drug reactions from medicines, vaccines, herbal products, biological medicines and product quality issues. Please fill in the information as complete as possible.

☑ I accept the terms & conditions

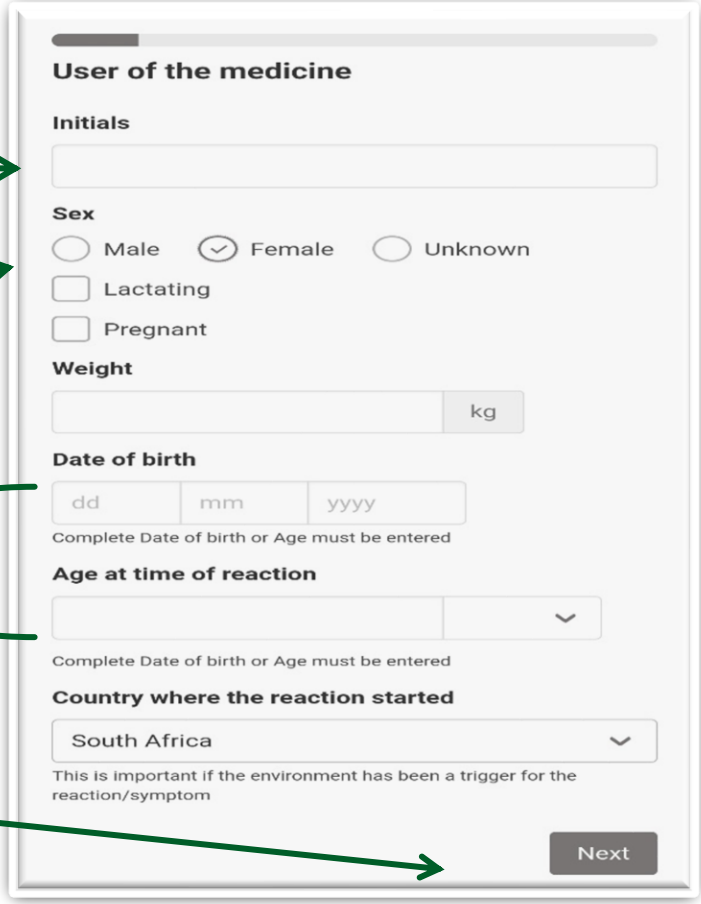
View the terms & conditions

I'm reporting for myself or a relative

I'm reporting as a health professional

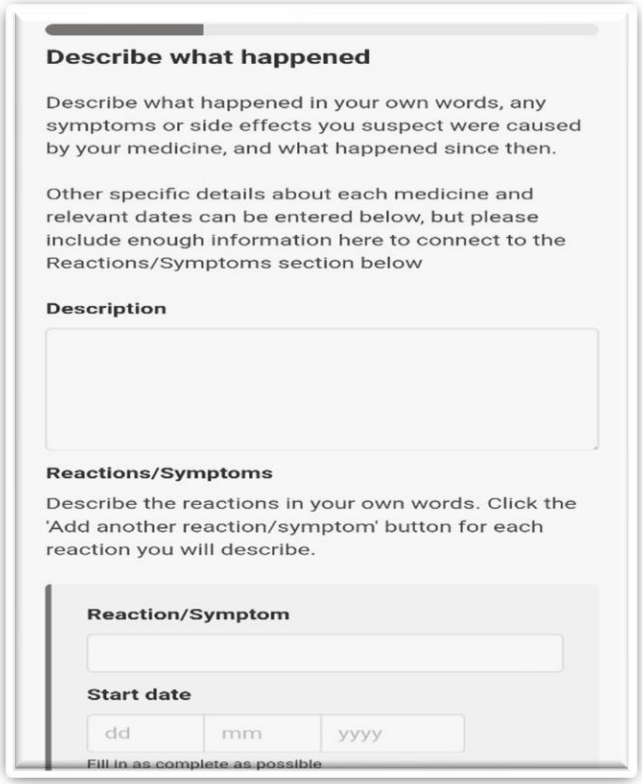
Navigation of e-Reporting Portal

- Patient's 1st name letters'; Helps in detecting duplicate reports or follow up of the same report
- If the patient's gender was female, mark if she is pregnant or lactating
- You can enter either the age at the time of the reaction or the date of birth
- Then tab "Next"

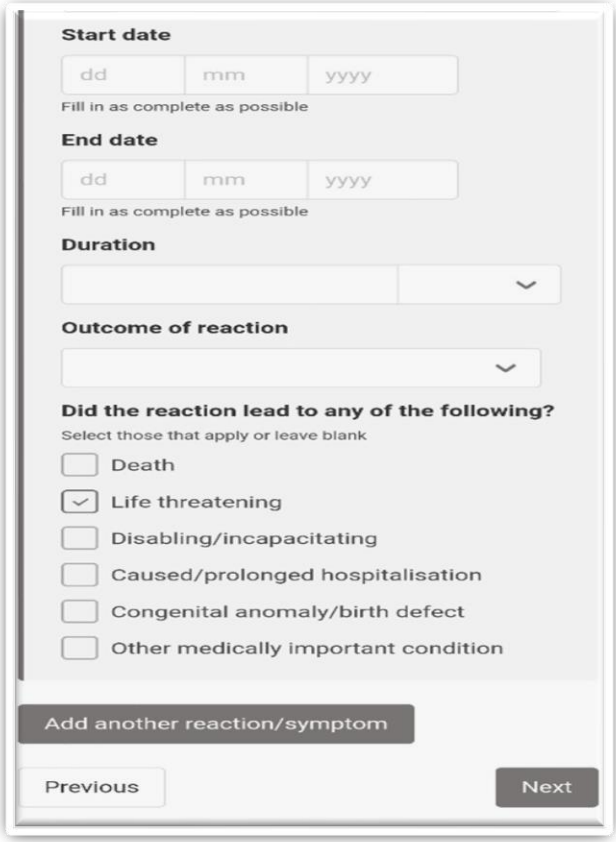


Navigation of e-Reporting Portal

Free text area to fill in here the reaction/ event

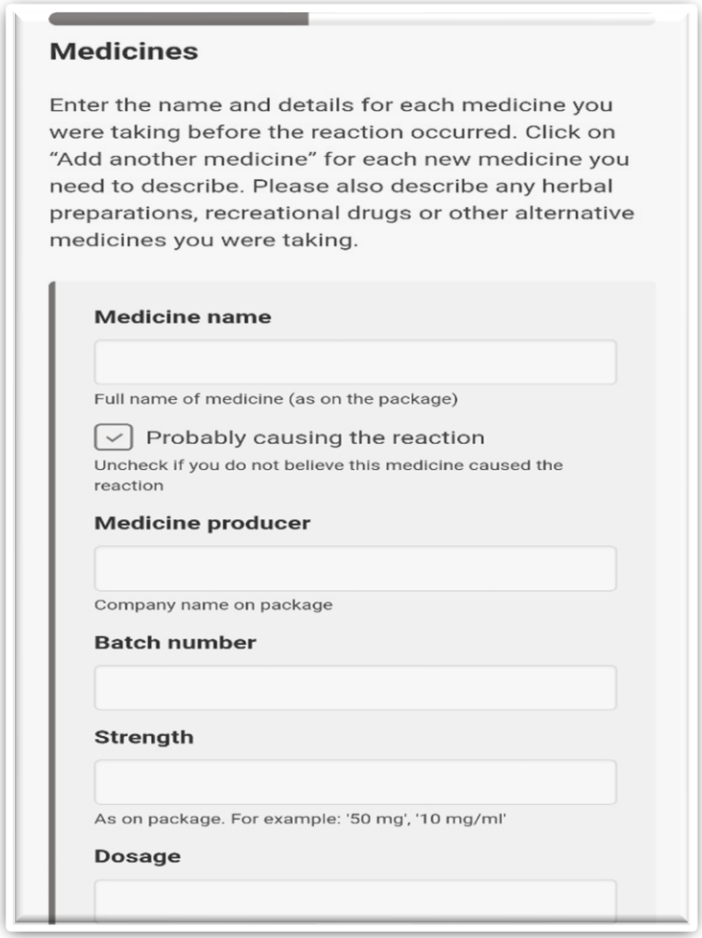


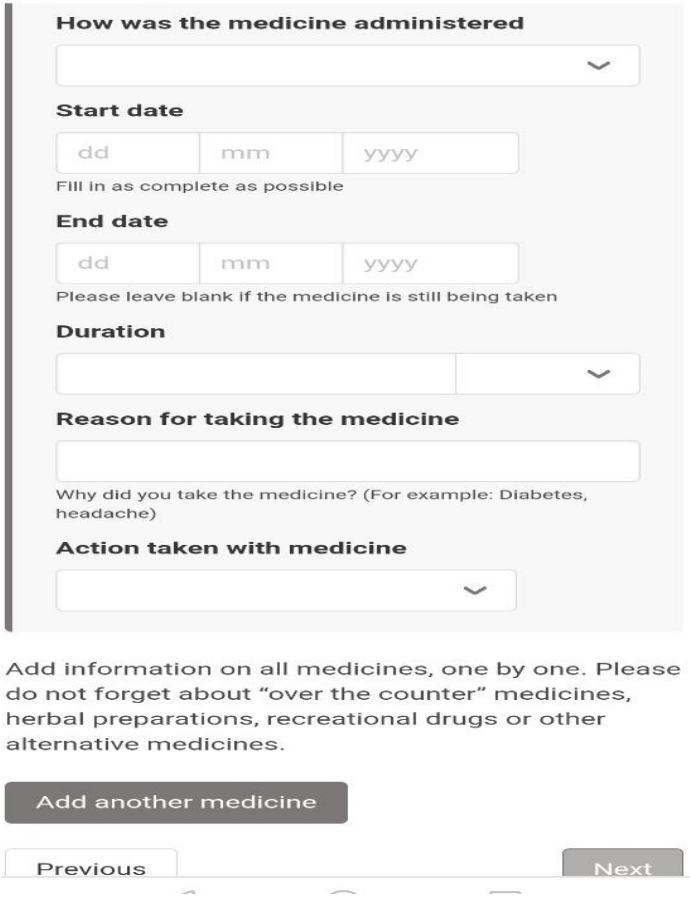
- You preferably enter full date, if you don't remember enter a month & a year or year only.
- Seriousness list will appear for each reaction
- Add more than reaction here
- Then click "Next"



Navigation of e-Reporting Portal

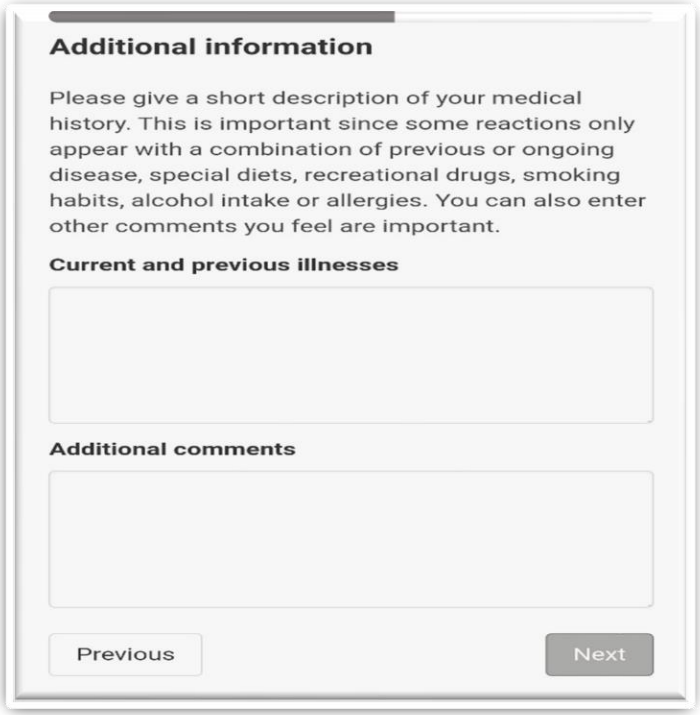
In case you are going to add concomitant medications “uncheck” this box





Navigation of e-Reporting Portal

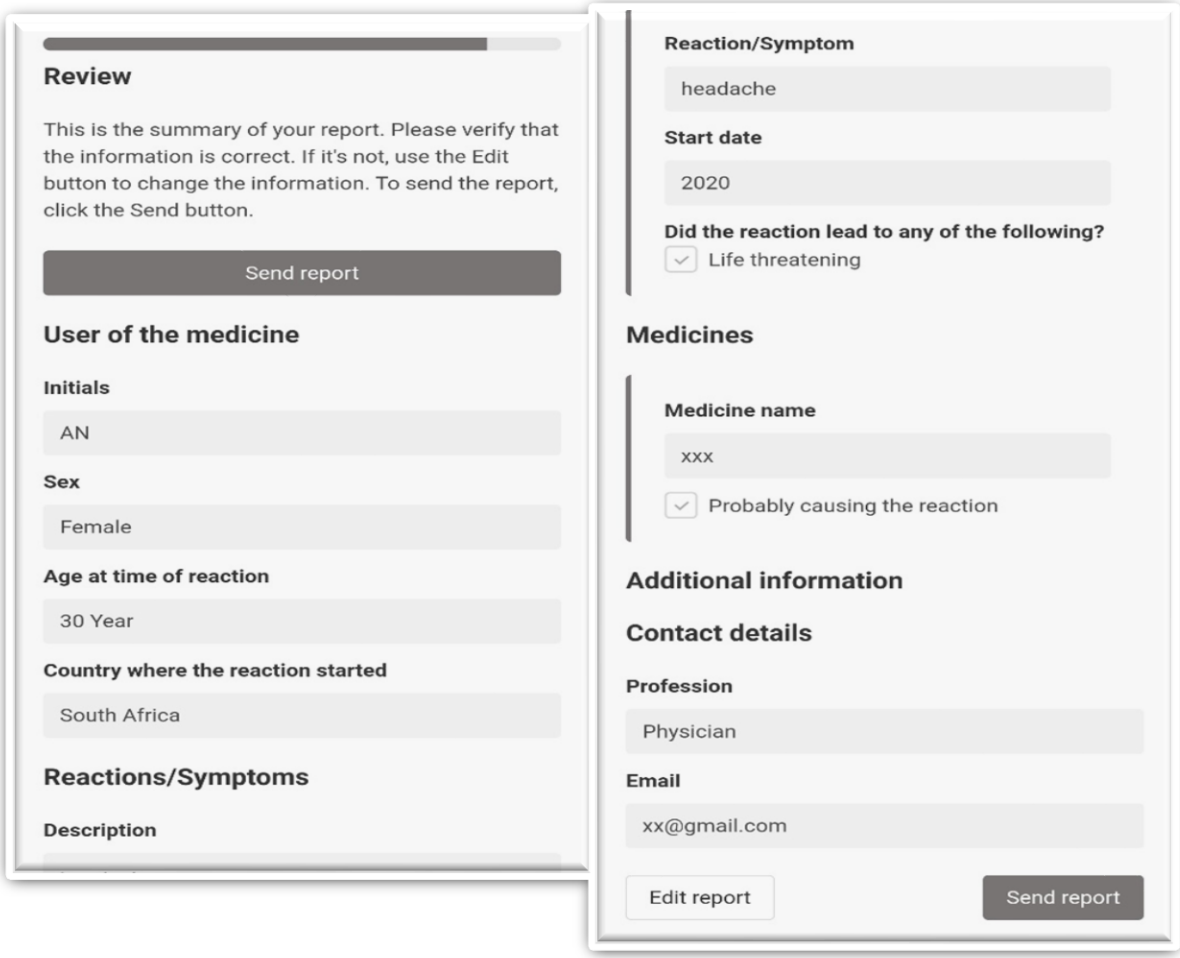
- Any additional information like previous illness, family history…



- Then the contact details of the reporter; you can either enter email or telephone number
- Click “Next” when you are done

Navigation of e-Reporting Portal

- Then you will be redirected to a page to review your entered data and you will need choose to “Edit report” or “Send report”



Navigation of e-Reporting Portal

- **Reference/ case number**

primaryreporting.who-umc.org/ZA

The report has been sent

Thank you for sending your report!

Case number: 10-930-516-372

Download report

10-828-181-289.pdf - Adobe Acrobat Pro DC

File Edit View Window Help

Home Tools Document 1 / 1

Report summary — South African Health Products Regulatory Authority, Case number: 10-828-181-289

User of the medicine

Initials	Sex	Weight	Date of birth	Age at time of reaction	Lactating	Pregnant	Country where the reaction started
VS	Female	56 kg	1 January 1999	22 Year	-	-	South Africa

Describe what happened

Description
Patient fainted after taking paracetamol

Reactions/Symptoms

Reaction/Symptom	Start date	End date	Duration	Outcome of reaction
allergic reaction	01 January 2023	-	- -	Recovering/Resolving
Did the reaction lead to any of the following?				
Life threatening				

Reaction/Symptom	Start date	End date	Duration	Outcome of reaction
dizziness	1 January 2023	-	- -	Recovered/Resolved
Did the reaction lead to any of the following?				
Other medically important condition				

Medicines

Medicine name		Batch number	Medicine producer	Reason for taking the medicine			
Paracetamol*		NFR2023	-	Headache			
Strength	Dosage	How was the medicine administered	Start date	End date	Duration	Action taken with medicine	

ADR & Quality Problem Reporting Form

- Fill in the required information as discussed in the previous reporting forms
- Should be sent to SAHPRA, Pretoria office by email: adr@sahpra.org.za; or to relevant pharmaceutical company (contact details found on the outer package of the health product).

Doc Number: GLF-CEM-PV-06A *[Old Doc no. 6.04]*	ADVERSE DRUG REACTION (ADR)/ PRODUCT QUALITY PROBLEM REPORT FORM (PUBLIC AND PRIVATE SECTOR) (Including Herbal Products)	SAHPRA South African Health Products Regulatory Authority
Revision: 2.0		Effective date: 20 January 2023

Reporting Health Care Facility/Practice

Building A, Loftus Park
402 Kirkness Street, Arcadia,
Pretoria
Tel: (012) 501 0311
E-mail: adr@sahpra.org.za

Facility/Practice | District | Province | Tel | Fax

Patient Details

Patient Initials | File/Reference Number | Date of Birth/Age

Sex ☐M ☐F ☐Unk | Race | Weight (kg) | Height (cm) | Pregnant? ☐N ☐Y

Allergies | Estimated Gestational Age at time of reaction

Suspect Medicine(s) [Medicines suspected to have caused the ADR], Concomitant [Other medicines taken together with the suspect medicine(s)] OR Interacting [Other medicines taken together with the suspect medicine(s) and may have interacted with the suspect medicine(s)] [Including over-the-counter and herbal products].

Trade Name (Active Ingredient if Trade Name is unknown)	Suspect or Concomitant or Interacting Medicines Taken (Please tick the applicable box)	Route	Dose (mg) and Interval	Date Started/ Given	Date Stopped	Reason for use	Batch Number	Expiry Date
	☐ Suspect ☐ Concomitant ☐ Interacting							
	☐ Suspect ☐ Concomitant ☐ Interacting							
	☐ Suspect ☐ Concomitant ☐ Interacting							
	☐ Suspect ☐ Concomitant ☐ Interacting							
	☐ Suspect ☐ Concomitant ☐ Interacting							
	☐ Suspect ☐ Concomitant ☐ Interacting							

Adverse Drug Reaction/Product Quality Problem

Date and time of onset of reaction | Date reaction resolved

Please describe Adverse Event/Product Quality Problem: (kindly add as much clinical information as possible)

Intervention (Tick all that apply)

☐ No intervention
☐ Intervention unknown
☐ Patient counselled/In-on-medical treatment
☐ Discontinued suspect drug; Replaced with: _____
☐ Decreased suspect drug dosage; New Dose: _____
☐ Treated ADR - with: _____
☐ Referred to hospital: Hospital name _____
☐ Other intervention (e.g., dialysis): _____

Patient Outcomes (Tick all that apply)

☐ ADR recovered/resolved
☐ Recovering/resolving
☐ Not recovered/not resolved
☐ Recovered with sequelae
☐ ADR resolved after suspect medicine was stopped: ☐N ☐Y
☐ ADR reappeared after restarting suspect drug/similar drug (rechallenge): ☐N ☐Y ☐Not done ☐Unknown

Adverse event seriousness criteria (Tick all that apply)

☐ Resulted in death
Date of death: _____
☐ Patient hospitalised or hospitalisation prolonged
☐ Life threatening
☐ Impairment/disability
☐ Congenital anomaly/ birth defect
☐ Other medically important condition

Laboratory Results

Lab Test	Test Result	Test Date

Additional Laboratory Results

Lab Test	Test Result	Test Date

Co-morbidities/Other Medical Condition(s)

Reported by

Name | E-mail

Designation ☐Nurse ☐Pharmacist ☐Doctor ☐Other: | Telephone

Date reported: | Signature

THIS ADR REPORT IS NOT A CONFIRMATION THAT THE REPORTER OR THE SUSPECT MEDICINE(S) CAUSED THE ADR

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ADR & Quality Problem Reporting Form

- Consent clause
- Other reporting tools
- Med Safety App
- SAHPRA online portal for products complaint:
- https://www.sahpra.org.za/complaints-relating-to-medicine-and-medical-devices/

ADVICE ABOUT VOLUNTARY REPORTING

Report adverse experiences with:
- medications (drugs, vaccines and biologicals)
- complementary / alternative medicines (including traditional, herbal remedies, etc.)

Please report especially:
- adverse drug reactions to newly marketed products
- serious reactions and interactions with all products
- adverse drug reactions which are not clearly reflected in the package insert.

Report Product Quality Problems such as:
- suspected contamination
- questionable stability
- defective components
- poor packaging or labelling
- therapeutic failures

Report even if:
- you're not certain the product caused the event
- you don't have all the details

Report Product Quality Problems via:
- phone: 0800 204 307
- SAHPRA portal: Complaints Relating to Medicine and Medical Devices - SAHPRA

Adverse Events Following Immunisation:
- phone: 0800 02 9999
- email: AEFI@health.go.za

Other reporting tools available at SAHPRA include:

Med Safety Application

The Med Safety Application is a mobile application designed for the public and healthcare professionals to report suspected ADRs/adverse event following immunisations (AEFIs). It is the preferred reporting tool by SAHPRA and allows for a seamless electronic submission of ADR/AEFI reports directly from the source into SAHPRA's reporting systems. The app can be downloaded onto a smart mobile phone directly from the SAHPRA website, https://medsafety.sahpra.org.za.
For more reporting channels please visit SAHPRA website, https://www.sahpra.org.za

CONSENT CLAUSE

By the signature above, the reporter hereby provides consent to the processing of personal information provided for the purpose of reporting a suspected adverse reaction. The reporter acknowledges that this information may be used a) to access all medical and clinical records for the purpose of gathering additional information for a clinical meaningful data, when required; b) in the generation of statistics; and c) to make policy decisions relating to safe use of medicines.

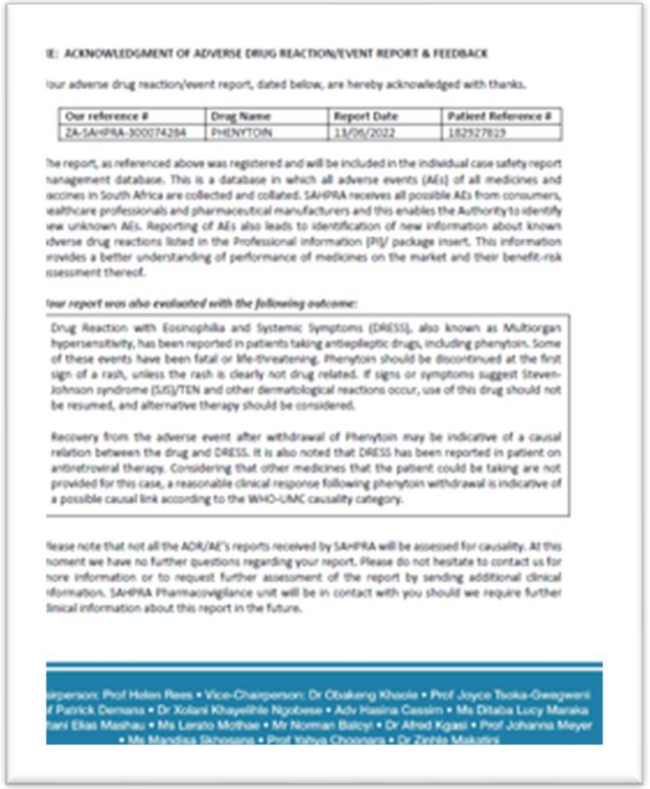
SAHPRA Vigilance unit undertakes to collate the personal information contained in this form and collected during the process of reporting of suspected adverse drug reaction in a manner that adheres to the Protection of Personal Information Act, so that your personal data is processed fairly, lawfully and transparently, adequate, relevant, and limited to what is necessary, processed for specific and legitimate purposes, accurate and kept up to date where necessary, kept in an identifiable form no longer than necessary for the purpose, processed securely . SAHPRA has put appropriate technical and organisational measures to safeguard your information. The information will not be stored for any longer than is necessary to achieve the purpose for which it was collected, unless SAHPRA Vigilance unit has a lawful basis to do so. If the reporter wishes to access and/or rectify their personal information, they may do so by contacting SAHPRA Vigilance unit at 012 501 0311 or via email: adr@sahpra.org.za.

Confidentiality: Identities of the reporter and patient will remain strictly confidential.

Your support of the South African Health Products Regulatory Authority's adverse drug reaction monitoring programme is much appreciated. Information supplied by you will contribute to the improvement of medicine safety and therapy in South Africa.

GLF-CEM-PV-06A_v2 Page 2 of 2

ADR Reporting Form Ack & Individualised Feedback



IE: ACKNOWLEDGMENT OF ADVERSE DRUG REACTION/EVENT REPORT & FEEDBACK

Your adverse drug reaction/event report, dated below, are hereby acknowledged with thanks.

Our reference #	Drug Name	Report Date	Patient Reference #
ZA-SAHPRA-300074284	PHENYTOIN	13/06/2022	182927819

The report, as referenced above was registered and will be included in the individual case safety report management database. This is a database in which all adverse events (AEs) of all medicines and vaccines in South Africa are collected and collated. SAHPRA receives all possible AEs from consumers, healthcare professionals and pharmaceutical manufacturers and this enables the Authority to identify new unknown AEs. Reporting of AEs also leads to identification of new information about known adverse drug reactions listed in the Professional information (PI)/ package insert. This information provides a better understanding of performance of medicines on the market and their benefit-risk assessment thereof.

Your report was also evaluated with the following outcome:

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as Multiorgan hypersensitivity, has been reported in patients taking antiepileptic drugs, including phenytoin. Some of these events have been fatal or life-threatening. Phenytoin should be discontinued at the first sign of a rash, unless the rash is clearly not drug related. If signs or symptoms suggest Steven-Johnson syndrome (SJS)/TEN and other dermatological reactions occur, use of this drug should not be resumed, and alternative therapy should be considered.

Recovery from the adverse event after withdrawal of Phenytoin may be indicative of a causal relation between the drug and DRESS. It is also noted that DRESS has been reported in patient on antiretroviral therapy. Considering that other medicines that the patient could be taking are not provided for this case, a reasonable clinical response following phenytoin withdrawal is indicative of a possible causal link according to the WHO-UMC causality category.

Please note that not all the ADR/AE's reports received by SAHPRA will be assessed for causality. At this moment we have no further questions regarding your report. Please do not hesitate to contact us for more information or to request further assessment of the report by sending additional clinical information. SAHPRA Pharmacovigilance unit will be in contact with you should we require further clinical information about this report in the future.

Your adverse drug reaction/event report, dated below, are hereby acknowledged with thanks.

Our reference #	Drug Name	Report Date	Patient Reference #
ZA-SAHPRA-300074424	CIPLA WARFARIN	28/06/2022	GT 40012931

The report, as referenced above was registered and will be included in the individual case safety report management database. This is a database in which all adverse events (AEs) of all medicines and vaccines in South Africa are collected and collated. SAHPRA receives all possible AEs from consumers, healthcare professionals and pharmaceutical manufacturers and this enables the Authority to identify new unknown AEs. Reporting of AEs also leads to identification of new information about known adverse drug reactions listed in the professional information (PI). This information provides a better understanding of performance of medicines on the market and their benefit-risk assessment thereof.

Your report was also evaluated with the following outcome:

Epistaxis is described in the PI/package insert of CIPLA WARFARIN. Most adverse events with warfarin are due to over-anticoagulation. It is important that the need for therapy is reviewed on a regular basis. This type of adverse drug reaction/event and the extent to which it occurs can be predicted. The CLEXANE therapy (concomitant medicine for this patient) may result in bleeding in the presence of associated risk factors such as organic lesions liable to bleed, invasive procedures or the use of medications affecting haemostasis. Warfarin concentrations may be affected when co-administered with Alavia. Recovery from bleeding after withdrawal of warfarin therapy may be indicative of a causal relation between the drug and bleeding. The raised partial thromboplastin time which subsequently decreased after warfarin treatment was stopped, and the INR result are indicative of over-coagulation effect. Bleeding stopped when Warfarin treatment was withdrawn while treatment with Clexane and other concomitant drugs were continued. Therefore, the causality assessment according to WHO-UMC causal link is Probable.

The SAHPRA Pharmacovigilance Team has also noted several ADR reporting forms indicating long or excessively long PT and INR in patients whose warfarin therapy is switched from one brand name to the other. This concern will be investigated further, and feedback will be provided in due course.

Please note that not all the ADR/AE reports received by SAHPRA will be assessed for causality. At this moment we have no further questions regarding your report. Please do not hesitate to contact us for more information or to request further assessment of the report by sending additional clinical information. SAHPRA Pharmacovigilance unit will be in contact with you should we require further clinical information about this report in the future.

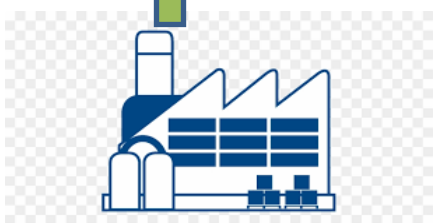
What happens to my ADR report?

WHO Programme for International Drug Monitoring (>30m ADRs from >170 countries)

SAHPRA
South African Health Products Regulatory Authority

E2B/ CIOMS reporting format

Reporters



Pharmaceutical industry

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

SAHPRA
South African Health Products Regulatory Authority

2030 NDP

Feedback received by Reporters?

- SAHPRA is constantly reviewing and updating product PI and PILs based on local and international safety data. New and updated medicines safety information can be accessed via the SAHPRA website, PI and PIL Repository (sahpra.org.za)
- Quarterly pharmacovigilance newsletters – SAHPRA - South African Health Products Regulatory Authority
- Safety-related regulatory decisions published on SAHPRA website - SAHPRA - South African Health Products Regulatory Authority
- Access to all reports available in the WHO global database (VigiAccess)
- Individualised feedback is provided to reporters, particularly for serious and unexpected reactions.
- Dashboard on AEFIs following COVID-19 vaccination - SAHPRA - South African Health Products Regulatory Authority

Protection of Reporters and Patients

- Protection of Persons Information Act Compliant (Act 4 of 2013)

  - ❑ Data is security and protection
  - ❑ Negligible risk of breach in confidentiality
  - ❑ Consent clause

- Reporting an ADR is blame free!
- NOT about finding fault.
- But protection of public safety!

Contact us

SAHPRA Pharmacovigilance Unit – Adverse events Reporting

Website:
https://medsafety.sahpra.org.za

Email: (manual ADR reporting forms & Follow-up reports)
adr@sahpra.org.za

Tel:
012 501 3011

Any Questions?