Title: Safe Use of Medicines in Zanzibar
A guide for health professionals in detecting and reporting adverse drug reaction.
(Beautiful photograph tablets and vials + syringe)
(First Draft)

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Acknowledgements

Introduction

The purpose of this Guide is to help health care providers at Primary Health Care Units (PHCU), Primary Health Care Centers (PHCC), District and Referral hospitals, including private practitioners to participate in the very important process of continuous observation of safety and effectiveness of the pharmaceutical products which are used in their clinical practice. Continuous evaluation of their benefit and harm will help to achieve the ultimate goal to make safer and more effective treatment available to patients.

Definitions

1. An adverse drug reaction (ADR) is ‘a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man’. In this description it is of importance that it concerns the response of a patient, in which individual factors may play an important role, and that the phenomenon is noxious (an unexpected therapeutic response, for example, may be a side effect but not an adverse reaction).

2. An unexpected adverse reaction is an adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorisation, or expected from characteristics of the drug.

3. A drug or medicine is ‘a pharmaceutical product, used in or on the human body for the prevention, diagnosis or treatment of disease, or for the modification of physiological function.

4. A side effect is ‘any unintended effect of a pharmaceutical product occurring at doses normally used by a patient which is related to the pharmacological properties of the drug’. Essential elements in this definition are the pharmacological nature of the effect, that the phenomenon is unintended, and that there is no deliberate overdose.

5. An adverse event or experience is defined as any untoward medical occurrence that may present during treatment with a medicine but which does not necessarily have a causal relationship with this treatment. The basic point here is the coincidence in time without any suspicion of a causal relationship.
6. A **serious adverse event** is any event that:
   - Is fatal
   - Is life-threatening
   - Is permanently/significantly disabling
   - Requires or prolongs hospitalization
   - Causes a congenital anomaly
   - Requires intervention to prevent permanent impairment or damage

7. A **signal** refers to ‘reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously’. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information.

**Rationale for safety monitoring of medicines**

There is very limited information available on ADRs in developing countries and countries in transition. However, one may expect that the situation is worse rather than better. This problem is also caused by a lack, in some countries, of legislation and proper drug regulations, including ADR reporting, a large number of substandard and counterfeit products circulating in their markets, a lack of independent information and the irrational use of drugs.

**The need for Pharmacovigilance in Zanzibar**

There are differences among countries (and even regions within countries) in the occurrence of ADRs and other drug-related problems. This may be due to differences in e.g.:

- diseases and prescribing practices;
- genetics, diet, traditions of the people;
- drug manufacturing processes used which influence pharmaceutical quality and composition;
- drug distribution and use including indications, dose and availability;
- the use of traditional and complementary drugs (e.g. herbal remedies *Give Zanzibar Experience*) which may pose specific toxicological problems, when used alone or in combination with other drugs. Data derived from within the country or region may have greater relevance and educational value and may encourage national regulatory decision-making. Information obtained in one country (e.g. the country of origin of the drug) may not be relevant to other parts of the world, where circumstances may differ. Therefore, drug monitoring is of tremendous value as a tool for detecting ADRs and specifically in relation to counterfeit and substandard quality products. ADR monitoring is to help ensure that patients obtain safe and efficacious products.

The results of ADR monitoring have also a very important educational value.

**How to recognize ADRs**
Since ADRs may act through the same physiological and pathological pathways as different diseases, they are difficult and sometimes impossible to distinguish. However, the following step-wise approach may be helpful in assessing possible drug-related ADRs:

- Ensure that the medicine ordered is the medicine received and actually taken by the patient at the dose advised
- Verify that the onset of the suspected ADR was after the drug was taken, not before and discuss carefully the observation made by the patient
- Determine the time interval between the beginning of drug treatment and the onset of the event
- Evaluate the suspected ADR after discontinuing the drugs or reducing the dose and monitor the patient’s status. If appropriate, restart the drug treatment and monitor recurrence of any adverse events
- Analyse the alternative causes (other than the drug) that could on their own have caused the reaction
- Use relevant up-to-date literature and personal experience as a health professional on drugs and their ADRs and verify if there are previous conclusive reports on this reaction. The National Pharmacovigilance Centre and Drug Information Centres are very important resources for obtaining information on ADR. The manufacturer of the drug can also be a resource to consult
- Report any suspected ADR to the person nominated for ADR reporting in the hospital or directly to the National ADR Centre

**Why reporting**

The information collected during the pre-marketing phase of drug development is inevitably incomplete with regard to possible ADRs. This is mainly because:

- Tests in animals are insufficient to predict human safety
- Patients used in clinical trials are selected and limited in number, the conditions of use differ from those in clinical practice and the duration of trials is limited
- By the time of licensing exposure of less than 5000 human subjects to a drug allows only the more common ADR to be detected
- At least 30,000 people need to be treated with a drug to be sure that you do not miss at least one patient with an ADR which has an incidence of 1 in 10,000 exposed individuals
- Information about rare but serious adverse reactions, chronic toxicity, use in special groups (such as children, the elderly or pregnant women) or drug interactions is often incomplete or not available

Thus, post-marketing surveillance is important to permit detection of less common, but sometimes very serious ADRs. Therefore health professionals worldwide should report on ADRs as it can save lives of their patients and others.
What to report?

For “new” drugs - report all suspected reactions, including minor ones. (In many countries drugs are still considered “new” up to five years after marketing authorization);

- For established or well-known drugs - report all serious or unexpected (unusual) suspected ADRs
- Report if an increased frequency of a given reaction is observed
- Report all suspected ADRs associated with drug-drug, drug food or drug-food supplements (including herbal and complementary products) interactions Report
- ADRs in special fields of interest such as drug abuse and drug use in pregnancy and during lactation
- Report when suspected ADRs are associated with drug withdrawals
- Report ADRs occurring from overdose or medication error
- Report when there is a lack of efficacy or when suspected pharmaceutical defects are observed.

Thus, report all suspected adverse reactions that you consider of clinical importance as soon as possible!

Who should report and to whom
ROLES AND RESPONSIBILITIES

Community/patients

- To report to health care providers on possible drug reaction
- Community leaders to sensitize the entire community on the importance of ADRs

TBAs/THs

- To encourage community members to report to the formal health care system when developing possible drug reactions

Private Sector

- To complete report form and submit to pharmacovigilance center

Expert Committee Drug Safety

- To review all possible drug reactions report forms and conduct causality assessment

National Coordinator for Pharmacovigilance
• To collect and store all possible drug reactions report at the center
• To communicate with all stakeholders such DHMT, DMU, UMC and others working in the field of Pharmacovigilance
• To carry out training to health care professionals

Drug Management Unit

To pursue any drug regulatory action proposed by Expert Committee Drug Safety
To communicate with manufacturers who have liability to the drugs.

Malaria Control Programme

• Assist with public information during the launching of new Antimalarial drug regimes
• To ensure training of health facility staff in use of antimalarial drugs

Media

• To deliver correct messages on the events to public

International Agencies

• To support national programmes throughout the process of establish, running, and reporting pharmacovigilant activities
• To collect international ADRs reports, provides methodological supports, analysis rates and risk-benefit profiles, and inform national pharmacovigilance of new serious adverse signals.
• To support expert panel to review periodically the safety profile of antimalarial drugs and provide technical guidance and possible training support to national essential drugs and malaria control programmes
How to complete report form: see example below (TO BE FILLED)

ZANZIBAR REVOLUTIONARY GOVERNMENT
MINISTRY OF HEALTH AND SOCIAL WELFARE
ZANZIBAR ADVERSE EVENTS REPORT FORM

**Patient Particulars**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref No.:</td>
<td>Age:</td>
</tr>
<tr>
<td>Date of birth:</td>
<td>Weight (kg):</td>
</tr>
</tbody>
</table>

If (female) is the patient pregnant

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Not sure</th>
</tr>
</thead>
</table>

If yes Date of Last Menstrual Period

<table>
<thead>
<tr>
<th>Date of Report</th>
<th>Date of Reaction</th>
<th>Duration</th>
</tr>
</thead>
</table>

**Reaction Details:**

**Suspected Reaction:** Brief description of reaction/side effects/drug interaction and laboratory results

**Suspected Drugs**

<table>
<thead>
<tr>
<th>Name</th>
<th>Date Started</th>
<th>Date Stopped</th>
<th>Daily dose.</th>
<th>Route</th>
<th>Disease/Condition</th>
</tr>
</thead>
</table>

**Other drugs used**
Describe how the reaction was treated

<table>
<thead>
<tr>
<th>Outcome of reaction</th>
<th>Recovered completely</th>
<th>Not yet recovered</th>
<th>Recovered with long term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of recovery</td>
<td>…/…/…..</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Remarks: eg include relevant medical history, drug allergy, previous exposure to similar drugs and other laboratory investigation

Reporter Details:

<table>
<thead>
<tr>
<th>Name</th>
<th>Qualifications:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address:</td>
<td>Tel no. if available</td>
<td>Signature</td>
</tr>
</tbody>
</table>

How to report ADRs?

Local Case Report Forms (CRF) should be obtained from the National Drug Regulatory Authority. Some countries have included CRF in their National Formularies (British National Formulary, Formularies of South Africa, Zimbabwe. There are different Case Report Forms in different countries. But all of them have at least four sections which should be completed:

1. Patient information:
   — patient identifier
   — age at time of event or date of birth
   — gender
   - weight

2. Adverse event or product problem:
   — description of event or problem
   — date of event
   — date of this report
   — relevant tests/laboratory data (if available)
   — other relevant patient information/history
   — outcomes attributed to adverse event

3. Suspected medication(s):
   — name (INN and brand name)
   — dose, frequency & route used
   — therapy date
   — diagnosis for use
   — event abated after use stopped or dose reduced
   — batch number
   — expiration date
   — event reappeared after reintroduction of the treatment
   — concomitant medical products and therapy dates
4. **Reporter:**
   — name, address and telephone number
   — speciality and occupation

   The completed Case Report Form should be sent to the Zanzibar Pharmacovigilance Center.

**Benefits of reporting**

The effectiveness of a national post marketing surveillance programme is directly dependent on the active participation of health professionals. Health professionals are in the best position to report on suspected ADRs observed in their every day patient care. All healthcare providers (physicians, pharmacists, nurses, dentists and others) should report ADRs as part of their professional responsibility, even if they are doubtful about the precise relationship with the given medication.

**Appendices**

- ADR report form
- Laboratory form
- Investigation form

**References**


Useful Websites

**WHO**
www.who.int/medicines/
Section: Quality Assurance and Safety: Medicines

**WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre)** www.who-umc.org