GUIDELINE ON PHARMACOVIGILANCE

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NATIONAL MEDICINE REGULATORY AUTHORITY
Norris Canal Rd, Colombo 01000, Sri Lanka

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PREFACE

Patients expect the medicines they receive to be safe and effective. Healthcare professionals expect the medicines they prescribe, dispense or administer are potentially safe. Safety of medicinal products is the primary concern of any Medicines Regulatory Body in the world. Although the duties, responsibilities and scopes of these different parties may be different invariably the objective of safety remains comparable. Being vigilance on medicinal product is an integral element towards assurance of the safety of medicinal products.

Success of any pharmacovigilance system depends on the generation of reports and the subsequent procedures. This document provides guidance to all the stake holders including NMRA, institutes and individuals who submit reports about their roles.

1. INTRODUCTION

National Medicines Regulatory Authority Act No. 05 of 2015 and rules and regulations thereof provide legal provisions for pharmacovigilance in Sri Lanka. Pharmacovigilance, as defined by the WHO is "the science and activities related to the detection, assessment, understanding and prevention of adverse drug effects or any other possible drug-related problems.

In line with this general definition it is clear that scope of pharmacovigilance is not limited to adverse reactions. It also includes lack of efficacy, medication errors, counterfeit medicines, abuse or misuse and interactions of medicines. On some occasions there may be an inter relation among these elements. For example, complaint received as an incident of lack of efficacy may be due to a counterfeit product. Cluster of adverse reactions may reveal a serious quality defect of a particular product. Irrespective of the type of the problem it affects the safety of medicines.

Underlying objectives of our pharmacovigilance system is preventing harm from adverse reactions or any other drug related problems and promoting the safe and effective medicines in particular through providing timely information about the safety of medicines to patients, healthcare professionals and the general public.

Ultimate objective of Pharmacovigilance is therefore safety of medicines.

Of late, number of New Chemical Entities and Similar Bio Therapeutic Products that received market authorization in Sri Lanka has been significantly increased. Due to the policy of the government to encourage local manufacturing of pharmaceuticals, considerable number of new manufacturers has emerged within the Island. In this scenario, strengthening Pharmacovigilance system in Sri Lanka has been a timely necessity.

2. OBJECTIVES OF ADVERSE DRUG REACTIONS MONITORING

1. Early detection of previously unknown adverse reactions
2. Recognition of increases in frequency of a known adverse reaction
3. Generate new hypothesis on ADRs that are specific to the local population
4. Quantitative analysis of benefit/risk ratio
5. Dissemination of information on ADRs for rational medicines prescribing and regulations
6. Identifying problems with batches or product of medicines

3. ABBREVIATIONS

ADRs - Adverse Drug Reactions

CEO - Chief Executive Officer

ICSR - Individual Case Safety Report

MEC - Medicines Evaluation Committee

MSD – Medical Supplies Division

NMQAL - National Medicines Quality Assurance Laboratory

NMRA - National Medicines Regulatory Authority

PV division – Pharmacovigilance Division

SAFRESC- Safety and Risk Evaluation Sub Committee

UMC - Uppsala Monitoring Centre

WHO - World Health Organization

WHO-ART - WHO Adverse Reaction Terminology

4. GLOSSARY OF TERMINOLOGY

Adverse Event:

Any untoward medical occurrence that may present during treatment with a medicine but does not necessarily have a causal relationship with the treatment

Adverse Reaction:

Any response to a drug which is noxious and unintended and occurs at normal doses

Causality Assessment

The evaluation of the likelihood whether a medicine was the causative agent of an observed adverse reaction.

Quality Failure

Any deviation of a genuine medicine authorized by the National Medicines Regulatory Authority, from the quality specifications set for them by the manufacturer specifications (official pharmacopoeia or in-house specification)

Serious Adverse Event:

Any adverse event that:

- Is fatal
- Is life threatening
- Is permanently/significantly disabling
- Require prolong hospitalization
- Causes congenital anomaly
- Requires intervention to prevent permanent impairment or damage

Side Effect:

Any unintended effect of a drug occurring at normal doses, which is related to the pharmacological properties of the Medicine

Unexpected Adverse Reaction

An adverse reaction the nature or severity of which is not consistent with domestic labeling or market authorization or expected from characteristics of the medicine.

Signal:

The term refers to reported information (at least 3 spontaneous case reports) on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously

5. PROCEDURE FOR REPORTING ADVERSE DRUG REACTION

Spontaneous reports are the main source of information in the pharmacovigilance system of Sri Lanka. This chapter explains the procedure for spontaneous reporting of adverse reactions.

ICSR forms for reporting ADRs is available on the web site of the NMRA (www.nmra.gov.lk) In addition, printed copies of the forms have been distributed among the pharmacy departments/sections of the Government Health Care Institutes. Requests from the Health care professionals or institutes for reporting forms should be made to the Pharmacovigilance Division of the NMRA.

6. INDIVIDUAL CASE REPORTING FORMS

ICSR forms have been designed to collect the essential information required for proper assessment of the ADR case report. Information to be filled in the ICSR forms can be categorized under the following headings.

- Information on the patient
- Information on the suspected medicine/medicines
- Description on the Adverse reactions
- Information on management of the adverse reactions.
- Information about the reporter

In order to overcome high level of missing data in the ADR reports on suspected anaphylactic reactions PV division has introduced a separate form for reporting of anaphylaxis which would capture all the important data.

7. PRIORITIES FOR REPORTING

Pharmacovigilance Division encourages to reporting even seemingly insignificant or common adverse drug events as it is required to establish a reporting culture in Sri Lanka. However, more emphasis should be made on the following categories.

- All suspected reactions for new medicines
- All serious or unexpected suspected reactions for established or well-known medicines
- Increased frequency of a given reaction
- All suspected ADRs associated with medicine– medicine, medicine – food or medicine – food supplements
- ADR on special field of interests such as medicine abuse and medicines used during pregnancy and during lactation
- Suspected ADRs associated with medicine withdrawals

- ADRs due to overdose or medication error
- Lack of efficacy or pharmaceutical defects

8. PROCESSING OF COLLECTED ADVERSE DRUG REACTION DATA

On receipt of a completed ICSR form the Pharmacovigilance pharmacist would ensure that the form has all the essential information before proceeding to perform the causality assessment. If the essential information is missing in the report PV pharmacist should contact the reporter and collect the necessary information to complete the form. Follow-up information can be obtained, via a telephone call and/or site visit and/or a written request. It is important to continue follow-up and report new information until the outcome has been established or the condition is stabilized.

PV pharmacist should inform the reporter/reporting institute to submit the samples of the suspected medicine directly to the NMQAL if it is required to do so. Samples should always be submitted with the required information.

It is important that at the time of the original report, sufficient details about the patient and reporter be collected and retained to enable future investigations.

Following the initial review Head of the PV division may take an immediate action such as withhold of the particular product as a precautionary measure where it is necessary. Approval of the CEO must be obtained prior to such action.

In case where expert opinions are required Head of the PV division can call for an immediate SAFREC meeting.

PV division should perform causality assessment for all serious ADR reports within 07 calendar days using appropriate tools. Where PV division is unable to reach a conclusion on the causality opinion of the SAFREC must be sought.

After causality assessment has been performed, the Head of pharmacovigilance should document all the findings and sign the form.

An acknowledgement letter or message should be sent to the reporter for every ADR report. The ADR reports shall be stored in a confidential database at the PV Division. All appropriate reports would be entered in the Global data base (VigiFlow)

9. WHO CAN SUBMIT THE REPORTS?

Medical Professionals preferably Doctors, Dentists, Pharmacists and Nurses can submit ADR reports to the PV division.

10. TIME LINES FOR REPORTING

Any suspected ADR should be reported as soon as possible. In case of serious adverse events reporting should be done within 24 hours. Delay in reporting will make reporting inaccurate and unreliable. If possible, report while the patient is still in the health facility this gives a chance to reporter to clear any ambiguity by re-questioning or examining the patient.

Additional sources of information

Complaints received from medical professionals, patients, mass media and the data base of the MSD may also trigger collection of further details.

11. SAFETY AND RISK EVALUATION SUB COMMITTEE (SAFRESC)

There would be an expert committee appointed by the NMRA which shall be named as Safety and Risk Evaluation Sub Committee (SAFRESC). The Committee provides advices and technical assistance to the division pertaining to the subject.

Members of the SAFRESC

1. Head of the PV Division
2. Two Pharmacologists from two different recognized universities in Sri Lanka
3. Two pharmacists attached to the PV unit
4. Immunologist, Medical Research Institute
5. Consultant Physician, NHSL
6. Director, NMQAL
7. Chief Pharmacist Technical Unit of NMQAL
8. Representative from the FHB
9. Representative from the Epidemiology Unit
10. A pharmacist representing MSD

Members of the SAFRESC would be appointed according to an approved procedure. Each appointment would be valid for a period of 3 years. Each member of the committee would be paid honorarium for attending the meeting. Meeting of the SAFRESC be hold on 3rd Thursday of every month at 2.00 pm. In case of an emergency Head of the PV Division can call an emergency meeting.

12. FEEDBACK

6.1 Staff and customers may provide feedback about this document by emailing info@nmra.gov.lk.

13.APPENDIX: ADR REPORTING FORMS

Appendix I
SUSPECTED ADVERSE REACTION TO MEDICINES/COMPLEMENTARY PRODUCTS/ MEDICAL DEVICES:

To be Filled in by the NMRA
REPORT NO:
STATE SECTOR: ☐
PRIVATE SECTOR: ☐

If you suspect and adverse event, please complete this white form. Do not put off reporting because some details are not Known. Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the adverse reaction. Identity of the patient and or/the reporter is kept strictly confidential.

A. PATIENT INFORMATION

BHT/ Prescription no/ Record no. (If applicable)	Name & address (optional):	Age /DOB	Weight	Sex ☐M ☐F	Ethnicity

B. SUSPECTED MEDICINE:

☐Generic name:	Dose,	Route ☐ ORAL ☐ IV ☐ IM ☐ Other Please specify.....	Therapy Dates (dd/mm/yyyy) Begun.:
Trade name			
Batch no			
Expiry date:			
Dosage form: Tablets, Capsules, Injections, Suspension.....	Frequency		Stopped:
Name and address of the manufacture			
	Diagnosis for use:		
B1 Click here add additional field if more than one medicines are suspected to be involved.			

C. DID THE PATIENT TAKE ANY OTHER MEDICINE/ VACCINE / TRADITIONAL MEDICINES IN THE LAST 3 MONTHS PRIOR TO THE REACTION? IF YES GIVE DETAILS

D. DETAILS OF THE ADVERSE REACTION

Date of onset of event dd/mm/yyyy:	Date of this report:
Time deference between the last dose and the onset of reaction (Days, Hours, Minutes, Seconds)	Lab investigations if any:

Describe event and treatment given :

Do you consider the reaction to be serious ☐ Yes ☐ No If yes please tick "✓" why the outcome of the adverse event is serious

Patient died due to the ADR ☐ Date :	Life threatening ☐ Medically significant ☐	Hospitalisation ☐ Hospitalisation prolonged ☐	Congenital anomaly ☐ specify):	Disability ☐ Permanent damage ☐	Required intervention to prevent permanent damage ☐

Result on discontinuation of suspect drug:√ ☐ Recovered ☐ Improved ☐ Disappeared ☐ Persisted ☐ Not Known	Result on reintroduction of drug Reappeared: Yes / No / Not known	Alternative diagnosis

Risk factors present: ✓

Renal dysfunction	Cardiac Dysfunction	Hepatic Dysfunction	Previous Allergies	Smoking	Alcohol	Drug addict	Pregnant	Other (name)

E. REPORTING DOCTOR/ PHARMACIST/ NURSE/DENTIST/ OTHER

Name ……
Designation:……
Address:……
Telephone number:……
Email :……
Signature:……

Institute
Hospital/Pharmacy/Clinic……
Ward No(If applicable)……
Date of reporting: …… / ……/….

Submit the filled form to the Pharmacovigilance Division, National Medicines Regulatory Authority, 120, Norris Canal Road Colombo 10. Fax: +940112689704. Tel: +940112698896/7

Appendix II

	ANAPHYLAXIS CASE REPORTING FORM **PINK FORM** ***(To be completed by a Medical officer)*** **Identity of the patient and the reporter is kept strictly confidential.**	**REPORT NO:** **To be filled in by the CDDA** **STATE SECTOR:** **PRIVATE SECTOR:**

If you suspect an allergic reaction (see definition of anaphylaxis at the end of page 2) related to a pharmaceutical product please complete this PINK FORM. Do not put off reporting because some details are not known. Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the anaphylactic reaction.

PATIENT DETAILS				
Name:			MOH Area:	RDHS Area:
Age	Sex	Ethnicity	Hospital:	BHT number:
Past allergic history: Has patient had previous allergic reactions? ☐ Yes ☐ No If 'Yes', Allergen is a ☐Drug (specify) ☐Vaccine (specify) ☐ Food/Other - specify?				

Part I: Clinical features						
Skin & Mucosa	☐ Urticaria ☐ Erythema ☐ Pruritus ☐ Prickle sensation				Specify the site of skin reaction:	
	Eye	☐ Red bilateral ☐ Red unilateral ☐ Itchy				
	Angioedema	☐ Tongue ☐ Throat ☐ Uvula ☐ Larynx ☐ Lip ☐ Face ☐ Limbs ☐ Other				
Respiratory system	☐ Sneezing ☐ Rhinorrhoea ☐ Sore throat	☐ Hoarse voice ☐ Stridor	☐ Sensation of throat closure ☐ Cough	☐ Tachypnoea ☐ Difficulty in swallowing	☐ Wheezing ☐ Indrawing / retractions ☐ Chest tightness	☐ Grunting ☐ Cyanosis ☐ Difficulty in Breathing
Circulatory System	☐ Measured hypotension (specify BP)		☐ Decreased central venous pulse		☐ Capillary refill time >3secs	☐ Tachycardia (specify rate)
CNS	☐ Loss of consciousness		☐ Distress	☐ Other(specify):		
GIT	☐ Diarrhoea	☐ Nausea		☐ Abdominal pain/cramp		☐ Vomiting
Diagnostic Criteria for anaphylaxis	☐ Rapid onset of occurrence of above sign & symptoms			☐ Two or more systems are affected		

PART 2: SUSPECTED PRODUCT AND EXPOSURE INFORMATION			
Date & Time of drug/vaccine administration: Date(dd/mm/yy) Time : am/pm			
Drug ☐ Oral ☐ Parenteral	☐ Vaccine	☐ Serum	☐1st dose ☐2nd dose ☐3rd dose ☐4th dose ☐Other
Generic name :	Trade name :		Dose (specify units,, mg, ml, mg/kg) and regimen
Batch/Lot number :	Expiry date :		For vaccine: VVM status I II III IV
If diluents used, specify batch number & expiry date:			
If parenteral medicine/vaccine: ☐ Single dose ☐ Multi dose			☐ Liquid ☐ Lyophilised
Route of administration: ☐ Oral ☐ IV ☐ IM ☐ SC ☐ ID ☐ Other(specify)			
Site of Administration: ☐ Deltoid ☐ Thigh ☐ Buttock ☐ Other (specify)			
Person who administered: ☐ Doctor ☐ Nurse ☐ PHI ☐ PHM ☐ Other (specify)			
Place of administration: ☐ Hospital ☐ MOH ☐ Clinic ☐ Private Hospital ☐ GP ☐ Other(specify)			

Part 3: Management	
Was Adrenaline administered? ☐ Yes ☐ No If 'Yes', Route : ☐ IM ☐ SC ☐ IV ☐ Other (Specify) Dose:……ml Place: ☐ Clinic ☐ Hospital ☐ Other (specify) Time:……am/pm Person who administered adrenaline: ☐ Doctor ☐ Sister/Nurse ☐ PHI/PHM ☐ Other	
Was a repeat dose of adrenaline given? ☐ Yes ☐ No	If 'Yes', describe
Were other medicines administered? ☐ Yes ☐ No	
Any other details concerning medicines/management (Including CPR)?	
Investigations	
	Blood taken for mast cell tryptase: ☐Yes ☐ No If 'Yes' specify the time interval after event: (Note:Serum Tryptase levels peak 60-90 min after the onset of anaphylaxis and persist to 6h. Therefore it is recommended that blood should be taken between 1 and 2 after the initiation of symptoms)
Part 4: Outcome	
Onset of first symptom: Date (dd/mm/yy) Time: am/pm ☐ Unknown	
Outcome: ☐ Full recovery ☐ Not fully recovered ☐ Recovered with sequelae ☐ Death Specify details:	
Time at outcome (recovery/death) Date (dd/mm/yy) Time: am/pm ☐ Unknown	
Highest impact of Adverse drug event/Adverse Event Following Immunization: ☐ Did not interfere with daily activities ☐ Interfered, but did not prevent daily activities ☐ Prevented daily activities	
Details of Reporting Source	
Name: Designation: Institute: Signature Date: Telephone:	

Send the filled form to Secretary, Safety of Medicines and Risk Evaluation Subcommittee (SAFRESC), Office of the Director MT&S 120, Norris Canal Road Colombo 10. Email: cdda@health.gov.lk. Fax: +940112689704. Tel: +940112698896/7.

Definition: Anaphylaxis is defined as a severe, life-threatening, generalized or systemic hypersensitivity reaction, characterised by rapidly developing life-threatening airway and/or breathing and/or circulation and or gastrointestinal problems usually (not always) associated with skin and mucosal changes.