

Sultanate of Oman
Ministry of Health
Directorate General of Pharmaceutical Affairs & Drug Control

Department of Pharmacovigilance & Drug Information

Guide for:

**Reporting Adverse Drug Reactions &
Quality Problems**

By Healthcare Professionals

Version 1, 2017

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1. Introduction

This Guideline has been developed by the Department of Pharmacovigilance & Drug Information (DPV&DI) to address the importance of pharmacovigilance to all healthcare professionals in the country. It gives an overview of what Pharmacovigilance is, how to detect and classify ADR. It also describes the role of **Regional Pharmacovigilance Centers** and reporting system to the Department of Pharmacovigilance & Drug Information (**National Pharmacovigilance Centre**).

The concepts and reporting requirements stated in this guideline are based mainly on the international guidelines of European Medicine Evaluation Agency (EMA), United State Food & Drug Administration (FDA), International Conference for Harmonization (ICH) and World Health Organization (WHO).

2. Pharmacovigilance

2.1 What is Pharmacovigilance?

According to the World Health Organization (WHO), Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.

2.2 Objectives of Pharmacovigilance

- ❖ To improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions.
- ❖ To improve public health and safety in relation to the use of medicines.
- ❖ To contribute to the assessment of benefits, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost –effective) use.
- ❖ To promote understanding , education and clinical training in pharmacovigilance and its effective communication to the public

3. WHO Programme for International Drug Monitoring

WHO Programme for International Drug Monitoring started in 1968, as a means of pooling existing data on ADRs. Currently, many countries participate in the programme (122 countries as in September 2015), which is coordinated by WHO together with Uppsala Monitoring Centre (UMC). As per the agreement between WHO and the government of Sweden, the WHO Headquarters is responsible for policy issues, while UMC is responsible for the operational issues.

The collaborating centre in Uppsala (UMC) is responsible for maintaining the global ADR database, Vigibase.

The WHO Collaborating Centre analyses the reports in the database to:

- Identify early warning signals of serious adverse reactions to medicines;
- Evaluate the hazard;
- Undertake research into the mechanisms of action to aid the development of safer and more effective medicines.

Through an advisory committee, WHO plays a major role in the provision of expert advice on all matters relating to the safety of medicines. The Committee facilitates consistent policies and action among member countries and to advise those who may be concerned about action taken in another country.

4. Department of Pharmacovigilance & Drug Information (DPV& DI)

To address the need of a system for routine drug safety monitoring and to ensure the protection of public health in Oman, Ministry of Health (MOH) joined WHO Programme for International Drug Monitoring in 1996, and in 2015, Department of Pharmacovigilance and Drug Information (DPV&DI) was established as the National Pharmacovigilance Centre . The DPV&DI is based within the Directorate General of Pharmaceutical Affairs & Drug Control (DGPA&DC) in the MOH.

The main goal of DPV & DI is to develop and implement pharmacovigilance and drug information systems that will provide unbiased information, monitor safety and effectiveness of pharmaceutical products, herbal medicines and health products in the country.

The main responsibilities of DPV& DI are:

- Collecting and analyzing case reports of ADRs and other drug problems such as drug quality and medication errors.
- Maintaining database of all drugs and pharmaceutical products.
- Coordinating with regional pharmacovigilance units in government health institutions in Oman and global pharmaceutical centers.
- Communicating of information about benefit, harm, effectiveness and risk about drug safety to healthcare professionals, patients and public.
- Preparing and circulating annual reports about all ADRs that occur in all health institutions in the country.
- Issuing and distributing Oman Safety Update Newsletter.
- Sending ADR reports to Uppsala Monitoring Center (UMC) in Sweden.

The responsibilities of Regional Pharmacovigilance Centers are:

- Collecting ADR reports from the hospital, pharmacy, wadrs, clinics etc..
- Sending all ADR reports and other drug problems such as drug quality and medication errors to DPV & DI.

5. Adverse Drug Reactions (ADR) and its types

4.1 Definition of ADR:

Adverse Drug Reaction (ADR) is a response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function.

4.2 Types of ADR

- **Type A effects**

Augmented pharmacologic effects - dose dependent and predictable (medicine actions) are those, which are due to (exaggerated) pharmacological effects. Type A effects tend to be fairly common, dose related (i.e. more frequent or severe with higher doses) and may often be avoided by using doses which are appropriate to the individual patient. Such effects can usually be reproduced and studied experimentally and are often already identified before marketing.

- **Type B effects**

Bizarre effects (or idiosyncratic) - dose independent and unpredictable (Patient reactions) characteristically occur in only a minority of patients and display little or no dose relationship. They are generally rare and unpredictable, and may be serious and are notoriously difficult to study. Type B effects are either immunological or non-immunological and occur only in patients, with - often-unknown - predisposing conditions. Immunological reactions may range from rashes, anaphylaxis, vasculitis, inflammatory organ injury, to highly specific autoimmune syndromes. In addition, non-immunological Type B effects occur in a minority of predisposed, intolerant, patients, e.g. because of an inborn error of metabolism or acquired deficiency in a certain enzyme, resulting in an abnormal metabolic pathway or accumulation of a toxic metabolite. Examples are chloramphenicol caused aplastic anaemia and isoniazid caused hepatitis.

- **Type C effects**

Chronic effects refer to situations where the use of a medicine, often for unknown reasons, increases the frequency of a "spontaneous" disease. Type C effects may be both serious and common (and include malignant tumors) and may have pronounced effects on public health. Type C effects may be coincidental and often concern long-term effects; there is often no suggestive time relationship and the connection may be very difficult to prove.

- **Type D effects**

Delayed effects (dose independent)

Carcinogenicity (e.g., immunosuppressants)

Teratogenicity (e.g., fetal hydantoin syndrome).

- **Type E effects**

End-of-treatment effects.

- **Type F effects**

Failure of therapy.

6. Spontaneous reporting of Adverse Drug Reactions

A spontaneous reporting of ADRs is a volunteer communication by healthcare professionals or consumers that describes one or more adverse drug reactions in a patient who was given one or more medicinal products and that does not derive from a study or any organized data collection scheme. It is the major source of information in pharmacovigilance.

In Oman, the yellow reporting ADR form (Annex 1) is used by DPV & DI to collect information on ADRs from healthcare professionals. Each ADR form concerns an individual Case Safety Report (ICSR).

6.1 Who should report an ADR?

➤ **Healthcare Professionals:**

- Physicians
- Pharmacists
- Dentists

- Nurses
- Other healthcare providers
- **Pharmaceutical Companies/ Marketing Authorization Holders (MAHs).**
- **All government hospitals, private hospitals, health centres, private clinics and private pharmacies.**

6.2 What to report?

- **Any undesirable adverse event suspected to be associated with use**
 - Drugs.
 - Herbal medicines
 - Health products
 - Biologicals (e.g. vaccines)
- **All ADRs as a result of prescription and non-prescription**
- **Unexpected reaction, regardless of their nature or severity, whether not consistent with product information or labelling.**
- **A serious reaction, whether expected or not.**
- **All suspected ADRs associated with drug-drug, drug-food or drug-food supplements interactions.**
- **An observed increase in frequency of a given reaction.**
- **Medication errors.**
- **Quality defects.**

6.3 How to report

- An Adverse Drug Reaction reporting form” yellow form”.
- Ministry of Health website (www.moh.gov.om).
- E-mail: mohphar@omantel.net.om.
- Mobile Smart application (eSehaty).
- DGPA & DC fax (22358489).

6.4 What information to Report

The four sections to validate ICRS are (*Annex 2 for detailed information required for ADR reporting*):

1. Patient information
2. Suspected drug (s)
3. Suspected adverse reaction (s)
4. Reporter information

6.5 When to Report

1. Report the adverse reaction immediately after it occurs.
2. If possible, take the decision to report whilst the patient is still with you, so that the details can be filled in at once on the reporting form.

6.6 How to recognize ADRs :

It is difficult and sometimes impossible to distinguish an ADR from the disease being treated since they may act through the same physiological and pathological pathways. However, the following approach is helpful in assessing possible drug-related ADRs:

1. Ensure that the medicine ordered is the medicine received and actually taken by the patient at the dose advised.
2. Take a proper history and do a proper examination of patient.
3. Establish time relationships by answering the following question:
“Did the ADR occur immediately following the medicine administration?
Some reactions occur immediately after the medicine has been given while others take time to develop.
4. Carry out a thorough physical examination with appropriate laboratory investigations if necessary.
5. Effect of Dechallenge and Rechallenge should be determined
 - **Dechallenge** (withdrawal of the suspected medicine)
 - **Rechallenge** (re-introducing the suspected medicine after a dechallenge): Rechallenge is only justifiable when the benefit of reintroducing the suspected medicine to the patient outweighs the risk of recurrence of the reaction, which is rare.
6. Check the known pharmacology of the medicine
 - Check if the reaction is known to occur with the particular suspected

medicine as stated in the package insert or other reference.

- **Remember:** if the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular suspected medicine.

6.7 Any negative consequences for reporting?

- The outcome of the report, together with any important or relevant information relating to the reported reaction, will be communicated to the reporter as appropriate.
- The details of the report are stored in a confidential database at the DPV & DI and the analyzed report will be sent to the Uppsala Monitoring Center (UMC).
- The names of the reporters or any other health professionals named on the report and the patient will be removed before any details about a specific adverse drug reaction is used or communicated to others.

6.8 What will happen to ADR report?

1. The submitted report will be entered into the national database for analyzing.
2. The information obtained from your reported reactions promotes the safe use of medicines on a local and international level.
3. A well-completed adverse drug reaction report submitted by you could result in any of the following:
 - additional investigations into the use of the medication
 - educational initiatives to improve the safe use of the medication
 - appropriate package insert changes
 - changes in the scheduling or manufacture of the medicine to make the medicine safer.
 - Other regulatory and interventions as the situation may warrant including recall/withdrawal.

7. Reporting of Quality Problems in medicinal products, herbal medicines and health products

A quality problem in a medicinal product herbal medicines and health products may be defined as an attribute of a medicinal product or component which may affect the quality, safety and / or efficacy of the product, and / or which is not in line with the approved marketing authorization for the product.

Classification of quality problems:

Critical quality problems: are potentially life threatening or could cause serious risk to patient health.

Major quality problems: are those which could cause illness or mistreatment but are not critical.

Minor quality problems: are those which are unlikely to pose a risk to patient.

7.1 Who should report a quality problem?

- **Healthcare Professionals:**
 - Physicians
 - Pharmacists
 - Dentists
 - Nurses
 - Other healthcare providers
- **Pharmaceutical Companies/ Marketing Authorization Holders (MAHs).**
- **All government hospitals, private hospitals, health centers, private clinics and private pharmacies.**

7.2 What to report?

- All medicinal products, herbal medicines, health products and biologicals.

7.3 How to report

- An Adverse Drug Reaction reporting form” yellow form”.
- Ministry of Health website (www.moh.gov.om).
- E-mail: mohphar@omantel.net.om.

- Mobile Smart application (eSehaty).
- DGPA & DC fax (24602287).

7.4 Types of quality Problems

- suspected mislabeled drugs
- packaging that is torn or punctured
- sterile containers or vials that are punctured or leaking
- packaging or product mix-ups
- Product difficulty in use:
 - Taste
 - Odour
 - Size
 - Opening
 - Closure
 - Storage
- capsule leakage
- chipped, cracked, or splitting tablets
- tablet or capsule discolorations
- broken, cracked, or chipped syringes
- suspected product contamination
- sterile syringes with floating objects or growth
- vials with foreign floating objects or growth
- leaking vials
- Packaging:
 - Look-alike
 - Outer pack
 - Inner pack
 - Cartons
 - Poor quality
 - labels
- Falsified medicines:

A falsified medicine is one with a false representation of:

(i) its identity, including its packaging and labelling, its name or composition as regards any of the ingredients including excipients and the strength of those ingredients;

(ii) its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorization holder; or

(iii) its history, including the records and documents relating to the distribution channels used.

7.5 What information to Report

- Product name (brand & generic), dosage form, strength
- Manufacturer(s)
- Pack size(s)
- Batch number(s)
- Number of units in the batch (es)
- As full a description of the defect as possible

7.6 What will happen to the report?

The submitted report will be entered into the national database for analyzing.

2. The information obtained from your reported reactions promotes the safe use of medicines on a local and international level.

3. Quality reports help identify trends and can lead to several types of actions:

- product recalls
- drug safety alerts
- product label changes
- withdrawal of products
- repackaging or reformulation of products

8. Glossary of terms used in Pharmacovigilance

Adverse Event (AE)

Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

Adverse Drug Reaction (ADR)

A response which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

An adverse drug reaction, contrary to an adverse event, is characterized by the suspicion of a causal relationship between the drug and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

Dechallenge

The withdrawal of a drug from a patient; the point at which the continuity, reduction or disappearance of adverse effects may be observed.

Drug/ 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.

Individual Case Safety Report (ICSR)

A report that contains ‘information describing a suspected adverse drug reaction related to the administration of one or more medicinal products to an individual patient...’

National Pharmacovigilance Centre

Refers to the Pharmacovigilance & Drug Information Department

Rechallenge

The point at which a drug is again given to a patient after its previous withdrawal.

Regional Pharmacovigilance Centre

Refers to pharmacy department of the hospital identified in the region for coordinating pharmacovigilance activities.

Serious Adverse Event or Reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose: results in

- Death

- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- is life-threatening

To ensure no confusion or misunderstanding of the difference between the terms ‘serious’ and ‘severe’, the following note of clarification is provided: The term ‘severe’ is not synonymous with serious. In the English language, ‘severe’ is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache). Seriousness (not severity) which is based on patient/event outcome or action criteria serves as guide for defining regulatory reporting obligations.

Side effect

Any unintended effect of a pharmaceutical product occurring at normal dosage, which is related to the pharmacological properties of the drug.

Spontaneous reporting

System whereby case reports of adverse drug events are voluntarily submitted from health professionals and pharmaceutical manufacturers to the national regulatory authority.

Unexpected adverse reaction

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

9. Abbreviations

ADRs: Adverse Drug Reactions

DGPA & DC: Directorate General of Pharmaceutical Affairs & Drug Control

DPV & DI: Department of Pharmacovigilance & Drug Information

ICRS: Individual Case Safety Report

MAH: Marketing Authorization Holder

MOH: Ministry of Health

PV: Pharmacovigilance

UMC: Uppsala Monitoring Center

WHO: World Health Organization

10. References

- Safety of Medicines, A guide to detecting and reporting adverse drug reaction. World Health Organization, Geneva 2002.
- The Importance of Pharmacovigilance, Safety Monitoring of medicinal products, World Health Organization, Geneva, 2002.
- Guidelines for Detecting & Reporting Adverse Drug Reactions Individual Case Safety, Reports For Healthcare Professionals, Rational Drug Use and Pharmacovigilance Department- JFDA (2014).
- Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Centre for Biologics Evaluation and Research (CBER). March 2005.
- ICH Topic E2E Pharmacovigilance Planning (Pvp), European Medicines Agency, June 2005.
- VOLUME 9A -of The Rules Governing Medicinal Products in the European Union– Guidelines on Pharmacovigilance for Medicinal Products for Human Use, (EMA) 2008.
- Guide to reporting of quality defects in medicinal products for human and veterinary use, March 2014, HPRA, Ireland.

11. Annexes

Annex 1: ADR reporting form (Yellow form)

Annex 2: Information required for ADR reporting

Annex 3: WHO codes for route of administration

Annex 1: ADR reporting form (Yellow form)

CONFIDENTIAL

**Suspected Adverse Drug Reactions (ADRs) & Drug Related Problems Reporting Form
Drugs/ Herbal Medicines/ Health Products/ Biological Products**

1 Patient Details

Patient initial(s): Date of Birth/Age: Sex: M F (Pregnant/ not pregnant)
 Weight (Kg):
 Nationality: M.R.No:

2 Suspected Medicine/ Herbal/ Health Product/ Biological

	Drug Name		Date started	End Date	Daily Dose	Dosage form	Route	BN	MF	Indication
	Trade	Generic								
Suspected										
Concomitant										

3 Suspected Reaction(s)/ Quality Problem(s)/ Medication Error(s)

Description of Reaction(s)/ Quality Problem(s)/ Medication Error (s):	Date of Onset: / /20 Date Stopped: / /20
	Outcome of Reaction: Recovered <input type="checkbox"/> Recovering <input type="checkbox"/> No Improvement <input type="checkbox"/> Fatal <input type="checkbox"/> Unknown <input type="checkbox"/>
	Seriousness of reaction: Patient died <input type="checkbox"/> Life-threatening <input type="checkbox"/> Permanently Disability <input type="checkbox"/> Hospitalization <input type="checkbox"/> Congenital Abnormality <input type="checkbox"/> Other <input type="checkbox"/>
	Additional Notes (medical history, test results, allergies, dechallenge, rechallenge, pregnancy etc. Attach papers if necessary)

4 Reporter Details

Name:		
Profession: <input type="checkbox"/> Physician <input type="checkbox"/> Pharmacist <input type="checkbox"/> Nurse <input type="checkbox"/> Dentist <input type="checkbox"/> Other		
HCP		
Address: Institution:	Governorate:	Wilayat:
Tel No:	Email:	
Signature:	Date:	

Kindly submit the report to:

Department of Pharmacovigilance & Drug Information
 Directorate General of Pharmaceutical Affairs & Drug Control, Ministry of Health
 P.O.BOX: 393, Muscat, PC: 100, Sultanate of Oman

Guide for Reporting Adverse Drug Reaction & Quality Problems

Phone: 22357688/ 22357687/ 22357686 Fax: 22358489;
Email: mohphar@omantel.net.om

Guidelines for Reporting

This form can be used by: <ul style="list-style-type: none">• Physician.• Pharmacist.• Dentist.• Nurses.• Other healthcare providers.	Use this form to report adverse drug reactions, medication errors & quality problems from: <ul style="list-style-type: none">• Drugs• Herbal Medicines• Health Products• Biological Products (e.g. Vaccines)
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Confidentiality: Reporter's and patient's identity are held in strict confidence by *Pharmacovigilance & Drug Information Department*, information provided by the reporter will be strictly protected and will not be used in any way against him / her.

Adverse Drug Reaction (ADR) is a response to a medicinal product which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the restoration, correction or modification of physiological function.

Medication Error: is an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient (prescribing, dispensing, storing, preparation and administration of a medicine).

Quality Problems:

- Suspected counterfeit product.
- Suspected contamination.
- Suspected pharmaceutical defects
- Product non-compliant with specification (chemical/ physical/ microbial)
- Poor packaging or labeling.
- Therapeutic failure.
- Others.....

Number of samples affected in the batch

Please provide sample

.....*Thank you*.....

Annex 2: Information required for ADR reporting

1. Patient information	<ul style="list-style-type: none">• Patient initials• Sex• Weight• Birth day or age
2. Suspected drug (s)	<ul style="list-style-type: none">• Name (Generic and brand name)• Strength (concentration)• Dose, Frequency• Dosage form• Route of administration• Indication for use• Duration of use, date started, date stopped• Batch number
3. Suspected adverse reaction	<ul style="list-style-type: none">• Description of the reaction• Seriousness of the reaction• Date the reaction started, stopped• Outcome of reaction• Treatment provided for the reaction• Additional notes (medical history, test results, allergies, dechallenge, rechallenge, pregnancy etc....)
4. Reporter information	<ul style="list-style-type: none">• Name, initials• Specialty• Address• Tel No & Email• Signature & Date

Annex 3: WHO codes for route of administration

ROUTES	CODES
Buccal	BU
Conjunctival	CO
Dental	DE
Implant	MP
Inhalation	IH
Insufflation	IS
Intra-arterial	IA
Intra-articular	IR
Intra-cardiac	IC
Intradermal	ID
Intramuscular	IM
Intranasal	IN
Intraperitoneal	IP
Intrapleural	IL
Intrathecal	IT
Intratracheal	TR
Intrauterine	IU
Intravenous	IV
Intravesical	IB
Per oral	PO
Per rectal	PR
Subcutaneous	SC
Sublingual	SL
Systemic (if route is not Specified)	SY
Topical (external)	TO
Transmammary transfer	TM
Urethral	UR
Vaginal	VA