Guidelines for Detecting & Reporting Adverse Drug Reactions

Individual Case Safety Reports
For Healthcare Professionals

Rational Drug Use and Pharmacovigilance
Department- JFDA

(2014)

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This Guideline for the Jordan Pharmacovigilance System has been developed to complement and support the efforts of orienting all healthcare professionals on the important concept of Pharmacovigilance. It gives an overview of what Pharmacovigilance is, how to detect and classify ADR's. It also describes the reporting system to the Jordan Pharmacovigilance Centre in the context of the Individual Case Safety Reports (ICSR). The reporting requirements stated in this guideline are based mainly on the guidelines of International Conference for Harmonization (ICH), the European Medicine Evaluation Agency (EMEA) the United States Food and Drug Administration (FDA), and Jordan Food and Drug Administration pharmacovigilance guidelines. Its ultimate goal is to enhance efforts in ensuring that safe, efficacious, and quality medicines are made available for all Jordanians.

All healthcare professionals are encouraged to actively participate in Pharmacovigilance and to report all suspected adverse drug reactions to help safeguard the patients' health.

Rationale Drug Use and Pharmacovigilance Department

Join us in having the right decision about medicines

Table of contents

Abbreviations

ADR Adverse Drug Reaction
CAPA Central Administration of Pharmaceutical Affairs
CIOMs Council for International Organizations of Medical Sciences
JPC Jordan Pharmacovigilance Centre
ICSR Individual Case Safety Report
MAH Marketing Authorization Holder
MOH Ministry of Health
PSUR Periodic Safety Update Report
PV Pharmacovigilance
SPC Summary of Product Characteristics
UMC Uppsala Monitoring Centre
WHO World Health Organization

What is Pharmacovigilance?

According to the WHO, Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine related problem.

Adverse drug reaction (ADR) Vs. Adverse Events

Adverse drug reaction is 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.

Adverse Event is any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this medicinal product.

An adverse drug reaction, is distinguished from the adverse event by; the former has a suspicion of a causal relationship between the medicinal product and the reaction, i.e. judged as being at least possibly related to the reaction by the reporting or the reviewing health professional, while the adverse event does not necessarily have such causal relationship.

Importance of Pharmacovigilance

The information collected during the pre-marketing phase is incomplete with regard to adverse drug reactions and this is mainly because:

- Patients used in clinical trials are limited in number and are not representative to the public at large. In addition, the conditions of use of medicines differ from those in clinical practice and the duration is limited.
- 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.

Therefore, post-marketing surveillance is important to permit detection of less common but sometimes very serious ADRs.

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.

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 Detect problems related to the use of medicines and communicate the findings in a timely manner,
- To contribute to the assessment of benefit, 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 health professionals and the public.

WHO Programme for International Drug Monitoring

As a means of pooling existing data on ADRs, WHO's Programme for International Drug Monitoring was started in 1968. Initially a pilot project in 10 countries with established national reporting systems for ADRs, the network has since expanded significantly as more countries worldwide developed national Pharmacovigilance centers for the recording of ADRs.
Currently, many countries participate in the programme, which is coordinated by WHO together with its collaborating centre in Uppsala, Sweden (UMC). The collaborating centre 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 an important role in the provision of expert advice on all matters relating to the safety of medicines. The Committee also exists to facilitate consistent policies and action among member countries and to advise those who may be concerned about action taken in another country.

Protecting patient confidentiality

Types of Adverse Drug Reactions

- **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 nonimmunological 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. Also 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 tumours) 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

Introduction to the Jordan Pharmacovigilance system

Jordan Pharmacovigilance Center (JPC) has been established in 2001 within drug directorate/ Ministry of Health to be responsible for the **collection** and **evaluation** of information on pharmaceutical products marketed in Jordan with particular reference to adverse reactions. Furthermore, JPC is taking all appropriate measures to:

a) Encourage physicians and other healthcare professionals to report the suspected adverse reactions to JPC and
b) Oblige marketing authorization holders to systematically collect information on risks related to their medical products and to transmit them to JPC.
c) Provide information to end-users through adverse drug reaction news bulletins, drug alerts and seminars.

JPC is handling these pharmacovigilance data in a way, which is compatible with the procedures undertaken by WHO Collaborating Center for International Drug Monitoring in order that pertinent data may be transferred between JPC and WHO center.

The following summarize the spontaneous reporting system procedure:

- A healthcare professional or marketing authorization holder reports a suspected adverse drug reaction related to one or more pharmaceutical products, to The Jordan pharmacovigilance center (JPC). Reports are made in writing (e.g. using report forms), electronically, or by any other approved way.
- Reports are collected, collated, and validated by the pharmacovigilance centre and are usually entered into a database. Serious reactions are handled with the highest priority.
- The database is used to identify potential signals and analyze data in order to clarify risk factors, apparent changes in reporting profiles etc.

Spontaneous reporting of Adverse Drug Reactions

The Spontaneous reporting structure is the **voluntary** and the most common way through which the regulatory bodies collect ADR information for medicines once they are on the market.
In Jordan the Yellow Card (a reporting form described below) is used by JPC to collect information on ADRs from healthcare professionals and members of the public. Each yellow card concerns an Individual Case experienced ADRs, thus it is also called Individual Case Safety Report (ICSR).

Individual Case Safety Report (ICSR)

A document providing the most complete information related to an individual case at a certain point of time. An individual case is the information provided by a primary reporter to describe suspected adverse reaction(s) related to the administration of one or more medicinal products to an individual patient at a particular point of time.

Who should report

Healthcare Professionals are the preferred source of information in pharmacovigilance, for example physicians, family practitioners, medical specialists, and dentists.
Nurses and other health workers may also administer medicines and should report relevant adverse drug reactions experienced by the patients.
Pharmacists can play an important role in the stimulation of reporting and in the provision of additional information (for example, on co-medication and previous medicine use).
Patients & their relatives can also report their experienced adverse drug reactions directly to JPC, or through their healthcare professionals. In this case seek the patient permission to contact their healthcare professionals for additional information and data verification.
Marketing authorization holder (MAH), being primarily responsible for the safety of their products, they are obligated to report **serious** adverse drug reactions they receive about their products to JPC. While the Non-serious ADRs should be included in the periodic safety update report (PSURs).

The Yellow Card and the Online Reporting

For the suspected adverse drug reaction to be reported; a unified form should be used to facilitate the reporting and to insure that the required information is included; therefore JPC has developed this unified reporting form (attached), it was adapted from the international Yellow Card.

This yellow card is to be used by the healthcare professionals and the patients while the Marketing authorization holders (MAH) should report the ICSRs using the International CIOMs form.
In addition, for most reporting convenience, a web-based dynamic reporting module was established for the easy report completion and online submission.

Characteristics of good case report

The quality of the reports is critical for appropriate evaluation of the relationship between the product and adverse reactions, thus good case reports include the following elements:
1. Description of the adverse reaction or disease experience, including time to onset of signs or symptoms and the seriousness of the reaction/s;
2. Suspected and **concomitant** medicines details (i.e., Name, concentration, dose, dosage form, rout of administration, indication for use, duration of use& batch number especially for vaccines), including over-the-counter medications, dietary supplements, and recently discontinued medications;
3. Patient characteristics, including the name or initials, age, sex, weight, and baseline medical condition prior to product therapy, co-morbid conditions, use of concomitant medications, relevant family history of disease, and presence of other risk factors;
4. Documentation of the diagnosis of the reactions, including methods used to make the diagnosis;
5. Clinical course of the reaction and patient outcomes (e.g., hospitalization or death);
6. Relevant therapeutic measures and laboratory data at baseline, during therapy, and subsequent to therapy, including blood levels, as appropriate;
7. Information about response to dechallenge and rechallenge; and
8. Any other relevant information (e.g., other details relating to the reaction or information on benefits received by the patient, if important to the assessment of the reaction).
The reporting form should be obtained from JPC, and at least **four sections** should be completed to have a **valid report**. In other words these four sections are the minimum information which allows the case report to be **valid** subsequently to be entered onto the national ADR database and become available for signal generation in order to facilitate evaluation of cases.
When one or more of these information are missing, the case should be followed up in order to validate the report and complete its processing as described above.

Yellow card is your window to communicate with us

The **four sections** to validate the individual case report (ICSR) are as follow:

An identifiable patient

- Patient initials
- Sex
- Weight
- Age at time of reaction or date of birth

Suspected medicine

- Name (INN and brand name)
- Strength (concentration)
- Dose, Frequency
- Dosage form
- Route of administration
- Indication for use
- Duration of use, date started, date stopped
- Batch number (especially for vaccines)

Suspected adverse reaction

- Description of the reaction
- Expectedness of the reaction (in accordance with the approved product information)
- Seriousness of the reaction
- Date the reaction started, stopped
- Outcomes attributed to adverse reaction
- Relevant tests/laboratory data (if available)

An identifiable reporter

- Name, initials
- Address
- Contact details
- Qualification (if healthcare professional)

What should be reported

If it is suspected that a patient has experienced an ADR it should be reported using a Yellow Card. ADRs resulting from prescription medicines, herbal remedies, and OTC medications can all be reported.. Causality does not need to have been established.

- For **new medicines** report all the suspected reactions, including minor ones. (medicines are considered "new" up to five years after marketing authorization)
- For established medicines or well-known medicines report **all serious** or unusual suspected adverse reactions, (see definition of a serious reaction, expectedness of reactions.
- Report if an **increased frequency** of a given reaction is suspected.
- Report all suspected ADRs associated with drug-drug, drug food or drug-food supplements (including herbal and complementary products) **interactions**.
- Report when suspected ADRs are associated with medicine withdrawals.
- Report ADRs occurring from overdose or **medication error**.
- Report ADRs in special fields of interest such as medicine abuse and medicine use in **pregnancy** (teratogenicity) and during lactation.
- In **children** under the age of 18, all suspected ADRs occurring, should be reported regardless of whether the medicine is licensed for use in children. Children are often not exposed to medicines during clinical trials and many medicines are used in children even if they are not licensed for this purpose. This means that monitoring of medicine safety is particularly important for this age group.

As soon as possible
Reports on all suspected adverse reactions

- known or not, serious or not – **are welcome and useful**
If there is any doubt about whether or not it is an ADR; always it is best practice to submit a report

How to recognize ADRs in patients

ADRs are difficult and sometimes impossible to distinguish 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

- A full medicine and medical history should be taken
- An ADR should be your first differential diagnosis at all times
- Ask if this adverse reaction can be explained by any other cause e.g. patient's underlying disease, other medicines including over-the-counter medicines or traditional medicines, toxins or foods
- It is essential that the patient is thoroughly investigated to decide what the actual cause of any new medical problem is.
- A medicine-related cause must be considered, especially when other causes do not explain the patient's condition

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:

- Remember: only a few medicines produce distinctive physical signs
- Exceptions include medicine eruptions, steroid-induced dermal atrophy, acute extra-pyramidal reactions
- Laboratory tests are important if the medicine is considered essential in improving patient care or if the laboratory tests results will improve management of the patient.
- Try to describe the reaction as clearly as possible- Where possible, provide an accurate diagnosis

5. Effect of Dechallenge and Rechallenge should be determined

- Dechallenge (withdrawal of the suspected medicine):
  Positive dechallenge is the improvement / resolution of ADR when the suspected medicine is withdrawn in a strong, though not conclusive indication of medicine induced reaction.

- Rechallenge (re-introducing the suspected medicine after a dechallenge)

Rechallenge is only justifiable when the benefit of reintroducing the suspected medicine to the patient overweighs the risk of recurrence of the reaction, which is rare. In some cases the reaction may be more severe on repeated exposure. Rechallenge requires serious ethical considerations**.**

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.

7. Report any suspected ADR to the person nominated for ADR reporting in the hospital or directly to the Jordan Pharmacovigilance Centre.

Seriousness of Adverse drug reactions

A serious adverse event or reaction is any untoward medical occurrence associated with the use of a medical product in a patient that at any dose, the outcome is one of the following:

1. Death

Report if the patient's death is suspected as being a direct outcome of the adverse reaction.

2. Life-Threatening

Report if the patient was at substantial risk of dying at the time of the adverse reaction or it is suspected that the use or continued use of the product would result in the patient's death.

3. Hospitalization (initial or prolonged)

Report if admission to the hospital or prolongation of a hospital stay results because of the suspected adverse reaction.

4. Disability

Report if the adverse reaction resulted in a significant, persistent, or permanent disability/ incapacity; (change, impairment, damage, or disruption in the patient's body function/structure, physical activities, or quality of life).

5. Congenital Anomaly

Report if there are suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child (birth defect).

6. Medically important event or reaction

Medical and scientific judgment should be exercised in deciding whether other situations should be considered serious such as important medical events that might NOT be

immediately life-threatening or result in death or hospitalization but might cause danger to the patient or might require intervention to prevent one of the other outcomes listed in the definition above.

Expectedness of the adverse drug reaction

The expectedness of the reaction is assessed in accordance with the approved product information; the reaction is **defined as expected** if it is included in package insert or the summary of product characteristics (SPC).
On the other hand the **unexpectedness** of the reaction includes the following:

- The reaction is not included in the package insert or the summary of product characteristics (SPC).
- The reaction is included in the package insert or the summary of product characteristics (SPC) but showed changes in its known frequency
- The reaction is included in the package insert or the summary of product characteristics (SPC) but showed changes in its known severity i.e. the change in the severity of a known adverse drug reaction is considered as unexpected to that medicine.

What are the benefits of these reports for the patients and the health care providers?

The reporting by the healthcare provider and patient is completely voluntarily, they will stand to benefit as:

- Improvement on the quality of care offered to patients
- Reduction of medicine related problems leading to better treatment outcome
- Improved patient confidence in professional practice.
- Access to feedback information on medicine related problems reported within the country and internationally
- Satisfaction for the fulfillment of a moral and professional obligation

Hand by hand to protect our families

Will reporting have any negative consequences on the reporter?

- 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 JPC 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.

How to obtain the reporting form

A web based dynamic reporting module is available at JPC website to be completed and submitted online. (www.jfda.jo)
At each hospital a Pharmacovigilance coordinator is assigned (preferred to be the clinical pharmacist, or the medicine information specialist), the reporting forms (yellow cards) are available at the hospital Pharmacovigilance coordinator for the hospital health care professional. Special stand for yellow cards is to be available in the community pharmacies (mainly for patients, community pharmacists & may be for the nearby private clinics).

How to submit ADR report

After filling the ADR reporting form; All ADR reports can be sent to the JPC by:

- **Submit on-line**: through the JFDA/ JPC website, a web based dynamic reporting module is available for completion online.
- **E-mail** : special account for ADR reporting, jpc@jfda.jo
- By **Hand:** contact person in hospitals, by pharmaceutical distribution companies….

There is collaboration between JPC and some pharmaceutical distribution companies to participate in collecting the filled ICSR then forward them to JPC.
While other reports can be submitted on regular basis (every month) by any of the above means.

Remember: the Basic principles of efficient reporting

In-time reporting

- Report the suspected adverse drug reaction as soon as it occurs- the report involves less work and is more accurate.
- Send the report quickly to the Jordan Pharmacovigilance center.

Strong suspicion and follow-up

- Continue your strong suspicion of the medicine-induced illness in the same patient and in other patients
- Keep a vigilance for signs and symptoms that may enhance or exclude the possibility of a medicine induced reaction
- All follow - up / supplementary information should be documented and submitted to the Jordan Pharmacovigilance center "FOLLOW - UP REPORT" clearly indicated on the top right corner of the form.
- Make sure that the patient names and patient code are the same in the 1st report & the Follow up report. As it is very important that follow-up reports are accurately identified and linked to the original report.

Accuracy and completeness

- Ensure that each reported Suspected ADR Reporting Form is filled in accurately and with all the necessary information, as much as is available to you. This is very important for assessing the causality of the medicine to have caused that reaction.
- Remember the 4 basic components that make a report reliable are:
  i. An identifiable patient
  ii. An identifiable health-care professional
  iii. An identifiable Adverse reaction or product problem
  iv. An identifiable medicine (suspected)

If the above information is missing, the report may not be useful.

- Remember to fill in all information accurately and in clear legible writing

Reporting an adverse event protects patient's life

Processing of Adverse drug reactions reports

What happens to the reported ADRs?

1. The information obtained from the report will be used to promote safe use of medicines in the local, national and international levels.
2. The submitted report will be entered into the national database of adverse drug reactions and be analyzed on a regular basis.

A well - completed and duly submitted ADR reported may result in:

- Additional investigations into the use of the medicine in Jordan
- Appropriate changes in the package insert
- Change the schedule of the medicine
- Enhancing educational initiatives to improve the safe use of that medicine
- Other regulatory and health promotion interventions as the situation may warrant including withdrawal / recall.

Causality assessment

Causality assessment is the method by which the extent of relationship between a medicine and a suspected reaction is established i.e. to attribute clinical events to medicines in individual patients or in case reports

The WHO scale of assessment and the Naranjo's scale are the most commonly used scales.

Glossary of important terms used in Pharmacovigilance

Adverse Event/ Adverse Experience

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

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.

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

Case Control Study
Study that identifies a group of persons with the unintended medicine effect of interest and a suitable comparison group of people without the unintended effect. The relationship of a medicine to the medicine reaction is examined by comparing the groups exhibiting and not exhibiting the medicine reaction with regard to how frequently the medicine is present.

Clinical Trial
A systematic study on pharmaceutical products in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reaction to investigational products, and/or to study the absorption, distribution, metabolism and excretion of the products with the objective of ascertaining their efficacy and safety.
Clinical trials are generally classified into Phases: I to IV. Phase IV trials are studies performed after marketing of the pharmaceutical product. They are carried out on the basis of the product characteristics for which the marketing authorization was granted and are normally in the form of post-marketing surveillance.

Cohort Study
A study that identifies defined populations and follows them forward in time, examining their rates of disease. A cohort study generally identifies and compares exposed patients to unexposed patients or to patients who receive a different exposure.

Causality assessment
The evaluation of the likelihood that a medicine was the causative agent of an observed adverse reaction. Causality assessment is usually made according established algorithms.

Drug/ Medicine
Any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient. The term drug/medicinal product is used in a wider sense to include the whole formulated and registered product, including the presentation and packaging, and the accompanying information.

Drug Alerts
The action of notifying a wider audience than the initial information holder(s) of a suspected association between a drug and an adverse reaction. Note that the term is used in different contexts that can be confusing, for example, an alert may be from a manufacturer to a regulator or from a regulator to the public.

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

Individual Case Safety Report (ICSR)
A document providing the most complete information related to an individual case at a certain point of time. An individual case is the information provided by a primary source to describe suspected adverse reaction(s) related to the administration of one or more medicinal products to an individual patient at a particular point of time.

Lack of Efficacy
Unexpected failure of a medicine to produce the intended effect as determined by previous scientific investigation.

National Pharmacovigilance Centre
A single, governmentally recognized centre (or integrated system) within a country with the clinical and scientific expertise to collect, collate, analyze and give advise on all information related to medicine safety.

Pharmacoepidemiology
The study of the use and effects of medicines in large numbers of people.

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

Prescription Event Monitoring
A system created to monitor adverse drug events in a population. Prescribers are requested to report all events, regardless of whether they are suspected adverse events, for identified patients receiving a specified medicine.

Rechallenge
The point at which a medicine is again given to a patient after its previous withdrawal. (see Dechallenge)

Record Linkage
Method of assembling information contained in two or more records, e.g., in different sets of medical charts, and in vital records such as birth and death certificates. This makes it possible to relate significant health events that are remote from one another in time and place.

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

- Death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/incapacity
- Congenital Anomaly
- Medically important event or reaction

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 reaction (as in mild, moderate or severe); the reaction itself, however, may be of relatively minor medical significance (such as severe headache).
Seriousness (not severity) which is based on patient/reaction outcome or action criteria serves as guide for defining regulatory reporting obligations.

Side Effect
Any unintended effect of a pharmaceutical product occurring at doses normally used in humans, which is related to the pharmacological properties of the medicine.

Signal
Reported information on a possible causal relationship between an adverse reaction 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 reaction and the quality of the reaction and the quality of the information.

Spontaneous Reporting
A system whereby case reports of adverse drug reactions 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 labeling or market authorization, or expected from characteristics of the medicine.

Every minute spent on reporting improves the quality of life of your patients

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Annex I: Yellow Card English

Annexe II: Yellow Card Arabic

Annex III: Our Publications

Pharmacovigilance Report Form
Report of Suspected Adverse Drug Reaction and Medical Related Problem

Note: Identities of Reporter, Patient and Institution will remain confidential

- Patient's Medical Record: ..... ☐ Male Weight:..... Kg Height:..... cm Age :..... Years

- Patient's Name/or Initials: ☐ Female Pregnant? ☐ Yes ☐ No Which trimester?.....

		Drugs by Brand Name	Manufacturer & Batch no.	Dosage Form & Route	Strength & Dose	Started on	Stopped on	Indications
Suspected Drugs	1-							
	2-							
	3-							
Other drugs	1-							
	2-							
	3-							

Suspected reactions/ Product Related Problem (Low efficacy, manufacturing defects.. etc.)	Date of onset	Duration of reaction
1-		
2-		
3-		

Comments (e.g. relevant history, allergies, previous exposure to the drug. ..... etc).

- Consequences of suspected reactions:-

Serious: ☐ Yes ☐ No. If serious please indicate the seriousness of reaction (s).

☐ Death (Date of death ..... Cause of death .....)

☐ Life threatening ☐ Hospitalization ☐ Leading to congenital anomaly

☐ Persistent disability ☐ Prolongation of hospitalization ☐ Other serious consequences (Specify .....)

- Outcome On The Day of Report:

☐ Recovered fully ☐ Recovered with reduced function ☐ Unknown consequence

☐ Full recovery is expected ☐ Death ☐ Other (Specify .....)

- Was Suspected Drugs (s) Discontinued? ☐ Yes ☐ No If yes, which drugs (s)?.....

- Did reaction(s) disappear after discontinuation of suspected drugs(s)?

☐ Yes ☐ No ☐ Unknown, if yes which reaction (s)? .....

- Did reactions(s) reappear after reintroduction of suspected drugs(s)?

☐ Yes ☐ No ☐ Unknown

- Reporter's Name & Status (Physician, Dentist, Pharmacist, Nurse) Office Address: .....

Date: ..... P.O. Box: ..... Phone: .....

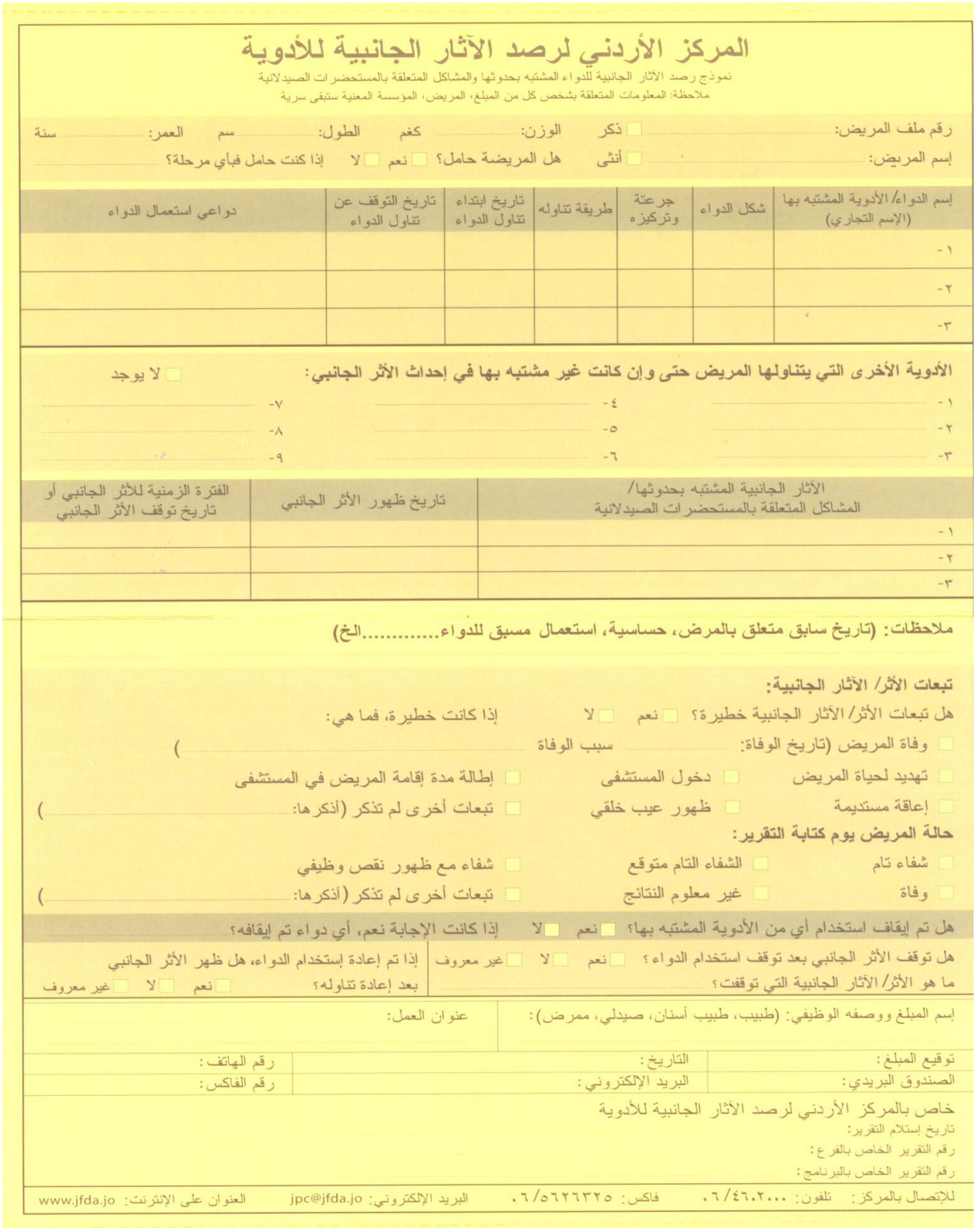
Reporter's Signature: ..... E-mail: ..... Fax: .....

For Jordan Food and Drug Administration.

Date of receiving the report:.....

Program report No.: .....

Note: in case there is additional information you can attach extra form.



المركز الأردني لرصد الآثار الجانبية للأدوية

نموذج رصد الآثار الجانبية للدواء المشتبه بحدوثها والمشاكل المتعلقة بالمستحضرات الصيدلانية
ملاحظة: المعلومات المتعلقة بشخص كل من المبلغ، المريض، المؤسسة المعنية ستبقى سرية

رقم ملف المريض: ذكر الوزن: كغم الطول: سم العمر: سنة
إسم المريض: أنثى هل المريضة حامل؟ نعم لا إذا كنت حامل فباي مرحلة؟

إسم الدواء/ الأدوية المشتبه بها (الإسم التجاري)	شكل الدواء	جرعة وتركيزه	طريقة تناوله	تاريخ ابتداء تناول الدواء	تاريخ التوقف عن تناول الدواء	دواعي استعمال الدواء
١-						
٢-						
٣-						

الأدوية الأخرى التي يتناولها المريض حتى وإن كانت غير مشتبه بها في إحداث الأثر الجانبي: لا يوجد

١- ٤- ٧-
٢- ٥- ٨-
٣- ٦- ٩-

الآثار الجانبية المشتبه بحدوثها/ المشاكل المتعلقة بالمستحضرات الصيدلانية	تاريخ ظهور الأثر الجانبي	الفترة الزمنية للأثر الجانبي أو تاريخ توقف الأثر الجانبي
١-		
٢-		
٣-		

ملاحظات: (تاريخ سابق متعلق بالمرض، حساسية، استعمال مسبق للدواء.....الخ)

تبعات الأثر/ الآثار الجانبية:

هل تبعات الأثر/ الآثار الجانبية خطيرة؟ نعم لا إذا كانت خطيرة، فما هي:

وفاة المريض (تاريخ الوفاة: سبب الوفاة)
تهديد لحياة المريض دخول المستشفى إطالة مدة إقامة المريض في المستشفى
إعاقة مستديمة ظهور عيب خلقي تبعات أخرى لم تذكر (أذكرها:)

حالة المريض يوم كتابة التقرير:

شفاء تام الشفاء التام متوقع شفاء مع ظهور نقص وظيفي
وفاة غير معلوم النتائج تبعات أخرى لم تذكر (أذكرها:)

هل تم إيقاف استخدام أي من الأدوية المشتبه بها؟ نعم لا إذا كانت الإجابة نعم، أي دواء تم إيقافه؟

هل توقف الأثر الجانبي بعد توقف استخدام الدواء؟ نعم لا غير معروف
ما هو الأثر/ الآثار الجانبية التي توقفت؟
إذا تم إعادة إستخدام الدواء، هل ظهر الأثر الجانبي بعد إعادة تناوله؟ نعم لا غير معروف

إسم المبلغ ووصفه الوظيفي: (طبيب، طبيب أسنان، صيدلي، ممرض):	عنوان العمل:
توقيع المبلغ:	التاريخ:
الصندوق البريدي:	البريد الإلكتروني:

رقم الهاتف:
رقم الفاكس:

خاص بالمركز الأردني لرصد الآثار الجانبية للأدوية
تاريخ إستلام التقرير:
رقم التقرير الخاص بالفرع:
رقم التقرير الخاص بالبرنامج:

للإتصال بالمركز: تلفون: ٠٦/٤٦٠٢٠٠٠ فاكس: ٠٦/٥٦٢٦٣٢٥ البريد الإلكتروني: jpc@jfda.jo العنوان على الإنترنت: www.jfda.jo

Volume 1, Issue 1
April 2014

JPVC NEWSLETTER

Jordan Pharmacovigilance center (JPVC), Rational drug use department

Special points of interest:

- Definition of rational use of medicies.
- Definition of pharmacovigilance.
- Pharmacovigilance (PV) at Jordan Food & Drug Administration.
- Newsletter opening

Inside this issue:

Rational drug use & pharmacovigilance department

Definition of rational use of medicies. "Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community." (WHO, 1985).

Jordan, is faced with the difficulties in providing equitable, evidence based and cost-effective health care within the limits of its ability to pay. About *7.7% of the Jordanian GDP is spent on health, *27% spent on drugs from which *45% in the public sector. (*From NHS 2013).

Rational drug use (RDU) department was established at August 2005 at Jordan food and drug administration (JFDA) to set up the plans for rationalizing medicines use in the public sector.

Definition of pharmacovigilance. " Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem." (WHO)

The aims of PV at JFDA are to enhance patient care and patient safety in relation to the use of medicines; and to support public health programs by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines. (JFDA).

PV was established within the drug directorate at 2001, then it became a member in the WHO At 2002, PV joined registration department at 2004 were they started their promotional campaign among health care provider to promote & encourage the reporting of adverse drug reactions (ADRs) to the companies & health care providers. PV guidelines first approved in June 2006, & it starts the evaluation of periodic safety update reports (PSUR) and risk management plans (RMP). The health hazardous evaluation committee was formed in 2008 to evaluate new ADRs & to take the appropriate regulatory action about them. Again the PV guidelines were updated in 2011.

The first Arabic PV guidelines issued at 2014.PV joined the RDU department at 2014.

Newsletter opening

Dear colleague's, Drug directorate is celebrating a new era through merging pharmacovigilance and rational drug use together in one department , due to our vision in the importance of reporting adverse drug reactions that enables us to build our own database which will be reflected in the future in taking the appropriate regulatory action toward medicines, also it will participate in decreasing drug cost during the government purchase of medicines, therefore we encourage you our colleagues doctors and pharmacist in the reporting of ADRs.

General director

Dr. Hayel obeidat

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August 2014

JPVC NEWSLETTER

Jordan Pharmacovigilance center (JPVC), Rational drug use department

المؤسسة العامة للغذاء و الدواء

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للإبلاغ عن الاثار الجانبية للأدوية الرجاء الدخول الى الموقع الالكتروني و الابلاغ عن طريق تعبئة نماذج الرصد الالكترونية المتصلة بقاعدة البيانات لدى مركز رصد الاثار الجانبية الأردني **(JPC)**.

Inside this issue:

Alkaptonuria (black bone disease)

Dr Mohammed Al-Sbou, Associate professor, Faculty of Medicine, Mutah University, Jordan.

Alkaptonuria (AKU) is a very rare metabolic disorder in phenylalanine and tyrosine catabolic pathway affecting 1 in 250,000. It is an autosomal recessive disorder characterized by accumulation of homogentisic acid (HGA) in the body, especially the connective tissues (cartilages, tendon and ligaments). This genetic disease is caused by mutations in the homogetisate 1,2 dioxygenase gene (HGO), which leads to the lack of homogentisate 1,2 dioxygenase enzyme activity. Excessive HGA is converted to a polymeric melanin-like pigment and binds to all connective tissues, this process is called ochronosis. The clinical manifestations of the disease are darkening of urine, which is usually presents at birth, ochronosis (blue-dark pigmentation of connective tissues) and ochronotic arthropathy, especially affecting the large weight-bearing joints and spine, these symptoms typically appear after the age of thirty. Complications of AKU begin after the age of fifty, these include stones formation (renal, prostatic, gall bladder and salivary), and cardiac valve involvement especially aortic valve disease. So far 626 patients with AKU have been identified in 40 different countries. In Jordan preliminary results of targeted family screening have identified 70 cases with AKU. This large number of AKU patients in a small country like Jordan, with a population of 7 million, is due to the high rateo consanguineous marriages. Recent published studies have reported forty cases with AKU in the southern region of Jordan. Most of these cases were undiagnosed or misdiagnosed and were found in specific families. For example, nine cases of AKU have been identified in one family. No effective treatment has been found so far for AKU. Treatment is primarily supportive, and includes pain management and physiotherapy. A drug called nitisinone, is the potential treatment for AKU. Severe cases of AKU require surgical intervention to replace the severely affected joints.

Picture of elbow joint from an AKU patient

JPVC NEWSLETTER

The aim of this Newsletter is to disseminate information on the safety and efficacy of pharmaceutical products, it provides you with the latest information on the safety of medicines and legal actions taken by regulatory authorities across the world.

It is also intended to promote the concept of pharmacovigilance and its importance to patient safety. The Newsletter will provide you with the latest news about the national pharmacovigilance center in Jordan (JPVC) and its activities.

Our great appreciations' & thanks to Dr Pia Caduff-Janosa & Dr Mohammad AL-Sbou for there valuable participation in our Newsletter. JPVC team "Ph.Nidaa Bwaresh, Ph.Ghadeer Al Qwasme, Ph. Jaber Jaber, Ph. Taqwa Maqatef "