GUIDELINE FOR

ADVERSE DRUG REACTION (ADR) REPORTING

Drug Administration and Control Authority
(DACA)
Addis Ababa
Ethiopia

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1. Introduction

Drug is a chemical substance or mixture of substances used in the diagnosis, treatment, mitigation or prevention of a disease. Drugs can be obtained from natural source (i.e. Plants, Animals, and Minerals) or they can be synthesized. Newly discovered drugs have to undergo a series of pre-clinical and clinical trials to prove its quality, safety and efficacy before market authorization.

The pre-marketing evaluation of drugs, which is limited, cannot guarantee absolute safety of drugs. And as it is not possible to eliminate all adverse effects of drugs, it is necessary to introduce a new drug after assessing its relative safety on the bases of risk/ benefit ratio.

Once a new drug is introduced for clinical use there may be a lot to find out about the health problems that it may cause in the future. Drug prescribed for treatment can cause a serious adverse reactions ranging from mere inconvenience to permanent disability and death.

Since drugs are intended to relieve suffering, patients find it peculiarly offensive that drugs cause disease, which are often unexpected. A simple account of unwanted effects as inherent to the drug is erroneous. In addition to the inherent factors, adverse effects are promoted or even caused by numerous non-drug factors.

ADR reporting and monitoring system is important to collecting, collating and analyzing data as a means of establishing new knowledge and generating early signals of possible drug complications not reported through clinical trials. Out put from such adverse drug reaction-reporting systems compliments the information appearing in the published literature and from other studies.

The drug policy of Ethiopia emphasizes that information about the harmful and beneficial effects of drugs shall be collected from health professionals and patients, relevant data compiled and analyzed and the findings be publicized at national and international level.

The drug administration and control proclamation No. 176/1999, article 20 gives the Drug Administration and Control Authority (DACA) the mandate to carryout post-marketing surveillance in order to ensure the safety, efficacy and quality of drugs that are put in to use. It also give the authority the power to ban the use, or revoke the registration, of drug that was put in to use when, later on, proved to be ineffective or its risks out weighs its benefits.

Collection, tabulation, and analysis of suspected adverse reaction on the national level is of paramount importance. Therefore, the authority has organized Adverse Drug Reaction monitoring (ADR) and promotion control division Under the Planning, Drug information establishment and dissemination Department.

The division has prepared an easy to fill in reporting form with prepaid postage and it will be available for all health professionals at each health institutions for voluntary and spontaneous reporting. The success of the ADR monitoring depends on the cooperation of the medical professionals in reporting suspected adverse reactions, especially to new drugs.

This guideline is prepared with the intention to make the reporting of ADR consistent, regular and complete. Hence, it gives information on what, when, how to report and to whom to report.

2. What is adverse drug reaction?

ADR is ***noxious*** and ***unwanted*** reaction to drugs that occurs at a ***dose used in human*** for diagnosis, treatment or prophylaxis. Many unwanted effects of drugs are medically trivial, and in order to avoid inflating the figures of drug- induced disease, it is convenient to retain the term side- effects for minor effects, which is related to the pharmacological properties of the drug.

The term adverse reaction should be considered for harmful or seriously unpleasant effects occurring at doses intended for therapeutic, prophylactic or diagnostic effect and which calls for reduction of dose or withdrawal of the drug and/ or forecast hazard from future administration.

3. Rationale of ADR monitoring

Reporting ADR is essential to obtain the necessary information on safety of products. It helps to detect adverse reaction, which were not observed on the development phase of a particular drug on population subgroup such as children, pregnant women, the old and patients with complicated disease, which are not normally exposed during the clinical trial. It is also essential for the early detection of unknown reactions and interactions, detection of increase in ADR frequency, identification and quantification of risk factors, detection of counterfeited and substandard drugs in the market.

4. Recognition of ADR

When an unexpected event, for which there is no obvious cause, occurs in a patient already taking a drug, the possibility that it is caused by a drug must always be considered. Distinguishing between natural progression of a disease and drug-induced deterioration is particularly challenging.

5. What to Report

Although there is a need to emphasize on adverse reaction to new drugs, unknown and unexpected adverse reactions, serious adverse reactions and suspected drug interactions, health professionals are generally requested to report all suspected adverse reactions to any therapeutic agent including vaccines, dental and medical supplies ranging from minor reactions to disability or death.

The reporter does not need to prove that there is a causal association between drug and adverse reaction. Therefore, uncertainty of the cause and effect relationship should not be reason for not reporting.

6. When to report

Any suspected ADR should be reported to the ADR monitoring division as soon as possible. Delay in reporting will make reporting inaccurate and unreliable. Reporting while the patient is still in the

health institution will give chance to the reporter to clear any ambiguity by re-questioning or examining the patient.

7. How to report

The spontaneous reporting system of adverse reactions is by far the most effective method of gathering such information. It is fairly efficient in detecting truly serious reactions. It appears that serious problems are reported early and that warnings are issued timely.

When there is an adverse reaction to drugs the reporting form (Annex I) should be completed by the concerned health professional and sent to the ADR monitoring division at DACA.

8. Direction for completing the ADR reporting form

8.1 General

The ADR reporting form (Annex I) comprise basic information about the patient, the drug, the adverse reaction, the action taken and the outcome

- The age, sex, description of the adverse reaction, information on suspected drug, and outcome are all considered essential and should be completed.
- The form should be completed by: Physicians, Health Officers, Dentist,..
- Complete the form to the best of your abilities.
- Avoid non-standard abbreviations.
- Use a separate form for each patient.
- Write legibly.

8.2 Specific

8.2.1 Reaction information

8.2.1.a. The patient's identity

Information about the patient's identity, nutritional status and habit should be provided. It is not necessary to write patient's full name. Use Patients name initials only. E.g. ASZ for Addis Solomon Zerga. The card number have to be stated as the card number and patient's identity are useful to solicit additional information if necessary and also for retrospective and prospective study of adverse drug reaction.

8.2.1.b. Description of the adverse reaction

Clear and brief description about the nature of adverse reaction than diagnosis, the date of onset, duration, time course and laboratory test results including "negative" and normal results of any relevant test performed should be reported. The severity of the reaction i.e. weather it has necessitated prolonged hospitalization or not, discontinuation of the drug or not, etc. have to be reported.

8.2.2. Information on the suspected drug

This information includes the identity and source of the drug, the dose, route of administration and the impact of withdrawal and re-administration of the suspected drug upon the adverse reaction.

8.2.2a). Drug Name

Use brand name of suspected drug(s). If generic name is used, specify the manufacturer of the drug. Avoid non-standard abbreviations such as PPF, CAF, MTC, TTC, etc.

8.2.2b). Dosage form and strength

The dosage form such as tablet, capsule, syrup, suspension, elixir, emulsion, injection, eye drop/ointment, topical crème/ ointment, otic drop, nasal drop, suppositories rectal/ vaginal etc. should be stated. The strength must also be expressed in metric system. e.g. 500mg tab, 250mg/5ml syrup,1gm rectal suppository etc. Sometimes strength can be expressed in % e.g. 2% hydrocortisone ointment.

8.2.2c). Frequency

Frequency of drug administration s should be clearly notified using standard abbreviations.

e.g. 3 times a day as tid or 8 hrly ,
2 times a day as bid or 12hrly,
4 times a day as qid or 6 hrly etc.

8.2.2d). Route

Route of administration expressed using standard abbreviation (Annex II). E.g. Per os as PO, Intra-muscular as IM, Intra-vascular as IV, Per-rectal as PR, Topical as TO etc.

It is also useful to indicate whether the medication is taken before or after meal using Latin abbreviations such as ac, pc etc.

8.2.2e) Date

The date the drug was started and discontinued is an important data to assess the cause and effect relationship of the drug and adverse reaction. Therefore it has to be stated clearly on the report form as date/ month/ year. If the drug has not been discontinued at the time of reporting, write continuing.

8.2.2f) Dechallenge and Rechallenge

If the reaction subside after discontinuation of the suspected drug (dechallenge), check Y (yes) and if not, check N (No). If the reaction reappear after the suspected drug is restarted (rechallenge), check Y (yes) and if not, check N (No). If there is no dechallenge and rechallenge then check NA (Not available).

8.2.2g) Drug used concurrently

List any other prescription or non- prescription drugs used concurrently with the suspected drug with all description i.e. brand name, route, dosage form, strength, frequency, indication, date started and date stopped. This information is useful for evaluation of possible drug interaction.

8.2.2h) Indication

Write the reason why the drug was used or the diagnosis for which the drug prescribed for both suspected drug and other drugs concurrently used.

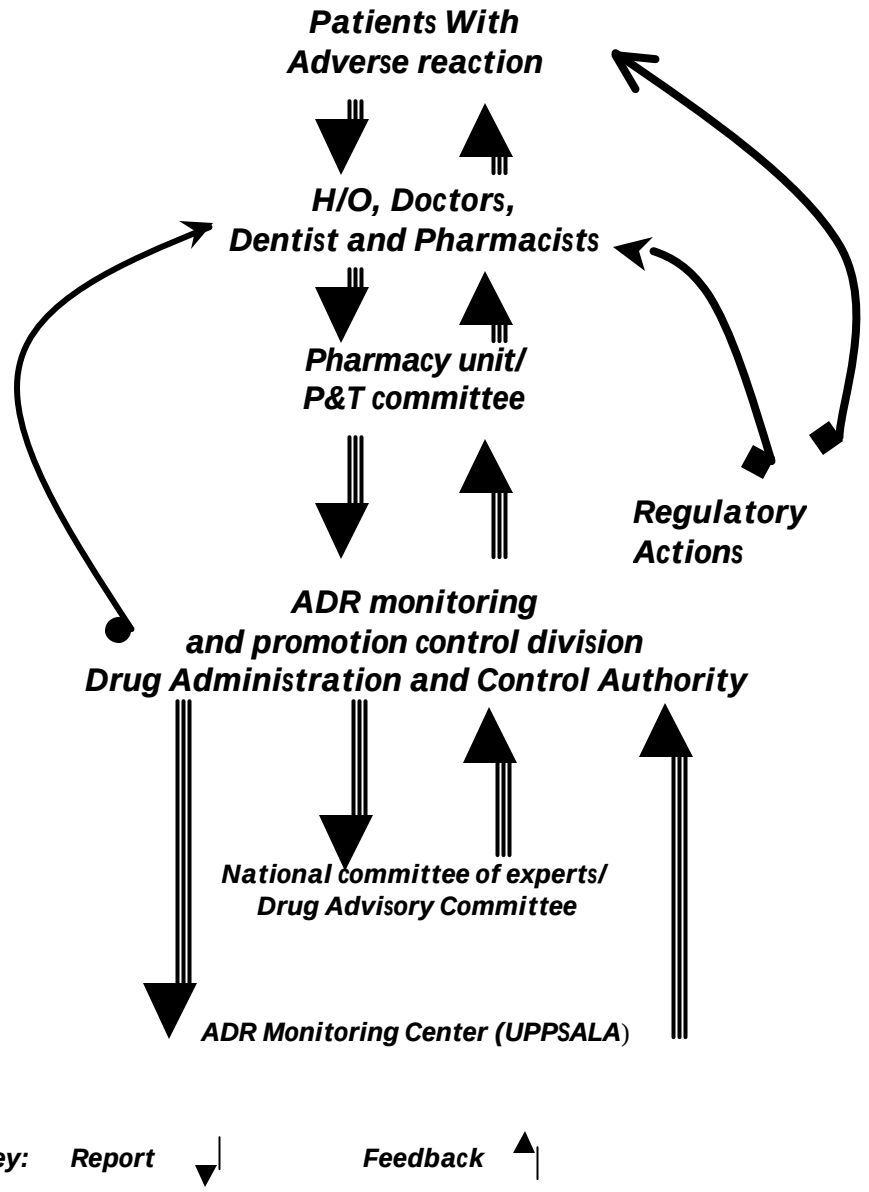
8.2.2i) Treatment

The treatment of the reaction, the final outcome of the reaction and sequelae has to be entered.

8.2.2j) Additional information

Any reaction the patient may have experienced previously, particularly similar to the current adverse event, either caused by the same or different drug has to be reported. Other relevant medical history, such as allergy, chronic disease, pregnancy and other factors, which may contribute i.e. herbal products, foods and chemicals, should be included under this heading. You may also add here why you think the adverse effect is due to the particular drug.

9. Schematic presentation of the ADR reporting system



10. Duties and responsibilities

10.1. Physician and other health professionals

- ❖ Report any suspected adverse drug reactions, drug interactions and unusual effects immediately.
- ❖ Fill the reporting form and hand over it to the pharmacy unit of the health institution.
- ❖ Give advice to patients on possible adverse drug reactions and drug interactions.
- ❖ Use drugs rationally.

10.2. Pharmacy unit

- ❖ Mail the ADR report to DACA.
- ❖ Retain the necessary documentation.
- ❖ Make sure availability of reporting form.
- ❖ Give advice to patients on possible adverse drug reactions and drug interactions.

10.3. Pharmacy and therapeutic committee

- ❖ Revise the drug list of health institution
- ❖ Promote rational use of drugs
- ❖ Distribute ADR information to the health professionals
- ❖ Ensure all the ADR report be kept confidential and identity of patients, reporters and trade names of the suspected drug not disclosed.

10.4. Drug Administration and Control Authority

- ❖ Promote reporting
- ❖ Collect report
- ❖ Give feedback
- ❖ Review the reported ADRs.
- ❖ Compile and analyze data collected
- ❖ Promote prevention of ADR and rational use of drugs
- ❖ Collect information on ADR and distribute to health professionals.
- ❖ Communicate with the international ADR monitoring center.
- ❖ Conduct research on ADR

- ❖ Ban the use or revoke the registration of drug, which is proved to have high risk than benefit.
- ❖ Take also other regulatory measures.

10.5. Drug advisory committee

- ❖ Evaluate *monitored adverse drug reactions* and
- ❖ Evaluate collected data
- ❖ Recommend on possible actions to be taken.

11. Evaluation of the ADR report

Reports are initially separated according to the source. All reports are individually evaluated. The team of experts at the ADR monitoring and promotion control division evaluates each report. It also examines the temporal relationship between the reaction and the drug, whether there was a positive dechallenge and rechallenge, the seriousness of the reaction, whether the current labeling lists the reaction, and whether the reaction is reported on medical literature.

Reaction to new medical entities and unexpected or serious reactions receive priority. If necessary, additional information may be solicited from the manufacturer or the reporter.

If similar cases are found, the reports become *a monitored adverse drug reaction*. The drug advisory committee evaluates monitored ADR, concurring medical literature, and reactions to drugs with in the same pharmacologic class and availability of additional databases for further investigation.

The committee will recommend action to be taken by the regulatory body on the particular drug with serious adverse drug reaction. These measures available are: withdrawal of the drug from the market, change on the product labeling and alert prescriber and consumer to the potential hazards of the medication or restrict the availability of the drug.

After a significant ADR is detected and a decision on the course of action determined, the information must be communicated rapidly and systematically.

12. Promotion of ADR reporting

In countries where there is an organized ADR monitoring, the number of ADR reported remained extremely low with in the medical profession. Most physicians considered ADR to be unexpected or harmful reactions; in fact half of them exclude well-established side effects as ADRs.

Though almost all physicians would take some action (i.e. withdrawing the drug or reducing the dose) when ADR occurred or suspected, only few would actually notify or seek advice. The most common explanation for the non-compliance in reporting ADRs was that unusual or serious reactions were infrequent and the assumption those common and trivial ones did not warrant reporting. The other factors were indifference, fear of personal consequence and uncertainty about what to report.

For the above reasons adverse drug reactions will remain largely outside the reach of monitoring agency. Therefore diverse understanding of the concept of ADR remains critical issue in the non-compliance of physicians in reporting ADRs. The pharmacy unit and pharmacy and therapeutic committee should exert effort to raise the interest of health professionals to report ADR and not to overlook the possibility of ADR.

It has to be known that data received by the national center will only be used for prevention of ADR and promotion of rational and safe drug use. It will not be made available to support any legal, administrative or other actions to the detriment of the reporting health professional, the patient or the coordinator. In this regard all the collected report will be kept confidential and identity of patients and reporter will not be disclosed. Publications will not disclose trade names unless regulatory actions have been taken.

Adverse Drug Reaction Reporting Form

'atient's Name: (Initials only)_____ Card Nº: _____ Age: _____ Sex:_____
Veight:_____ Habit: _____ Address: _____

Adverse Drug Reaction Description (Including Laboratory test results) Date of onset of Reaction: _____/_____/____
_____
_____
_____
_____
_____
_____
_____
_____

Reaction necessitated: Discontinuation of drug/s/ ☐ Yes ☐ No
Prolonged Hospitalization ☐ Yes ☐ No

Information on Suspected Drug						
Drug Name (use Brand Name . if generic name are used ease indicate manufacturer and batch no. if applicable.)	Route	Dose	Frequency	Date Drug		Therapeutic Indication
				Started	Stopped	
				D|M|Y	D|M|Y	
Other Drugs Taken Including self-medication						

Reaction subside after D/C of Suspected Drug ☐ Y ☐ N ☐ NA
Reaction reappear after Restart of Suspected Drug ☐ Y ☐ N ☐ NA
Treatment of reaction:
_____
_____
_____
_____

Outcome: ☐ Died due to adverse reaction ☐ Died, drug may be contributory ☐ Died Unrelated o drug
☐ Not yet recovered ☐ Recovered with out sequelae ☐ Recovered with sequelae ☐ Unknown
Sequelae: _____

Additional information: (e.g. relevant history such as allergies, chronic disease, pregnancy etc.)
_____
_____
_____
_____
_____

Reported by: Name _____ Profession: _____ Signature: _____ Date: _____
Name of health Institution: _____ Address: _____ Tele Nº: _____

Continued

For office use only

Received On: _____ Registration Nº: _____

Key: D|M|Y Date |Month |Year; D/C Discontinue Treatment; Y Yes; N No; NA Not available

What to report
All suspected reactions to drugs
Unknown or unexpected ADRs
Serious adverse drug reactions
Unexpected therapeutic effects
All suspected drug interactions

From _____

_____

_____

_____

_____

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Drug Administration and Control Authority
ADR Monitoring & promotion control Division,
P. O. Box 5681,
Addis Ababa,
Ethiopia

Annex III. Latin Terms and Abbreviations

1. Dosage forms

Latin Name	Abbreviation	English Name
Auristillae	Auristill	Ear drops
Capsuta	caps.	A capsule
Collutorium	Collut	A mouth wash
Collyrium	Collyr	An eye lotion
Cremor	Crem.	A crem
Emulsio	emul.	An emulsion
Gragarisma	grag.	A grag
Gelatinia	gelat.	A jelly
Inhalatio	inhal.	An inhalation
Injectio	inj.	An injection
Linctus	linct	A linctus
Linmentum	lin.	A liniment.
Liquor	liq.	A solution
Lotio	Lot	A lotion
Mistura	m./mist.	A mixture
Naristillae	narist.	Nasal drops
Nebula	neb.	A spray solution
Oculetum	oculent.	An eye ointment
Pessus	pess	A pessary
Pigmentum	pigm	A paint
Pilula	pil.	A pill
Suppsitorim	suppos	A suppository
Tab ella/Tabletta	tab	A tablet
Trochiscus	troch.	A lozenge
Ungueentum	ung.	An ointment
Vapor	Vpa	An inhalation

2. Time of Administration or Application

a) Time per day

Terms or phrase	Abbreviation	Meaning
Semel in die/ Semel die	sem. in die/ sem. die	Once a day
Bis in die, Bis die	b.i.d, b.d	Twice a day
Ter in die, Ter die,	t.i.d, t.d	Three times a day
Quater in die, Quater die	q.i.d, q.d	Four times a day
Sexies in die, Sexies die	sex.In d., sex.d.	Six times a day
Bis terve in die,	b.t.i.d.	Two or three times a day
Ter quaterve in die,	t.q.d.	Three or four times a day
Ter die sumendus,	t.d.s.	Three times daily
Quarter die sumendus,	q.d.s.	Four times daily
Quarta quaque hora	q.q.h.	Every four hours
Quotidie	quot.	Daily
Ter quotidie	ter quot.	Three times daily
Vices	vic	Time, times
Ad tres vices	ad 3 vic	For three times

b) Parts of the day

Terms or phrase	Abbreviation	Meaning
Prima luce	prim. luc.	Early in the morning
Primo mane	prim. m.	Early in the morning
Mane	m.	In the morning
Omni Mane	o.m.	Every morning
Nocte	n.	At night
Omni Nocte	o.n.	Every night
Hora decubitus	h.d.	At bed time
Hora somni	h.s.	At bed time
Nocte et Mane	m.et.m.	Night and morning
Nocte maneque	n.m.	Night and morning
Hac nocte	hac noct.	To-night
Cras vespere	cras.vesp.	Tomorrow evening
Mane sequenti	m.seq.	The following morning

c) **'Hour' Time**

Omni hora quaque	o.h.qq.h	Every hour
Omni quarta hora	o.q.h	Every fourth hour
Omni quarta hora	o.q.h	Every fourth hour
Singulis horis	sing.hor.	Every hour
Secundis horis	sec.hor.	Every two hour
Alternis horis	alt.hor.	Every two hour
Tertiis horis	tert.hor.	Every three hour
Quartis horis	quart.hor.	Every four hour
Sexis horis	sext.hor.	six hour

d) **Correlated time**

Terms or phrase	Abbreviation	Meaning
Ante cibos, Ante cibum	a.c.	Before meals, Before food
Post cibos, Post cibum	p.c.	After food, After meals
Inter cibos, Inter cibum	i.c.	Between meals, Between food

e) **Other terms**

Terms or phrase	Abbreviation	Meaning
Cum	c	With
Sine	s	without
Dolore	dol.urg.	when the pain is severe
Frequenter	freq.	Frequntly
Pro re nata	p.r.n	Occasionally (when required)
Quoties opus sit	quot.o.s	As often as necessary
Si dolor urgent	si dol.urg.	If the pain is severe
Si opus sit	s.o.s	when required, when necessary
Statim	stat	Immediately at once
Tussi urgent	tuss.urg.	When/If the cough is troublesome
Per os	p.o.	by mouth
	Rep repeat	