Guidelines on submitting periodic safety update report and any other reports that may be relevant to determine the safety, efficacy and quality of a drug

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Authorization of these guidelines

	Authorized by
Title	Secretary to the Authority
Name	Donna Kusemererwa
Signature	
Date	12th April 2018

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Part 1: Introduction

1.1 The mandate of National Drug Authority

National Drug Authority (NDA) was established in 1993 by the National Drug Policy and Authority Statute, which in 2000 became the National Drug Policy and Authority (NDP/A) Act, Cap. 206 of the Laws of Uganda (2000 Edition). The Act established a National Drug Policy and National Drug Authority to ensure the availability, at all times, of essential, efficacious and cost-effective drugs to the entire population of Uganda, as a means of providing satisfactory healthcare and safeguarding the appropriate use of drugs. Regulation 37 (hereinafter referred to National Drug Policy and Authority (Monitoring of Adverse Drug Reactions) Regulations, 2013) provides for assessing on-going safety of products as one of the ways of achieving this mandate.

This document describes the requirements set by NDA, for Marketing Authorization Holders (MAH) to submit on-going safety data to enable continual decisions on risk-benefit of registered products.

1.2 Definitions

The definitions provided below apply to the words and phrases used in these guidelines.

"Act" means the National Drug Policy and Authority Act

"Ad hoc PSURs" means reports outside the routine reporting requirements, and may be requested by NDA.

"Adverse drug reaction" means a response to a drug 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 modification of physiological function;

"Applicant" means a person who applies for registration of a medicinal product to NDA, who must be the owner of the product. He may be a manufacturer or a person to whose order and specifications, the product is manufactured. After the product is registered, the applicant becomes the Marketing Authorisation Holder (MAH).

"Authority" means the National Drug Authority;

"*Counterfeit drug*" means a drug which is deliberately or fraudulently mislabeled with respect to its identity, content or source;

"Data lock point" means for a periodic safety update report (PSUR), the date designated as the cut-off date for data to be included in a PSUR.

"Drug" means any substance or preparation used or intended to be used for internal or external application to the human or animal body either in the treatment or prevention of disease or improving physiological functions.

"Individual case safety reports" means format and content for the reporting of one or several suspected adverse reactions to a medicinal product that occur in a single patient at a specific point of time

"International birth date" means the date of the first marketing authorisation for a medicinal product in any country in the world

"Licensed person" means a person licensed under section 14 of the Act;

"Periodic safety update report" means a report on the safety experience of a drug at defined times, after the drug is registered (SI-regulation);

"Pharmacovigilance" means the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug related problem.

1.3 Abbreviations and acronyms

DIBD	Development International Birth Date
DLP	Data Lock Point
DSUR	Development Safety Update Report
IBD	International Birth Date
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
MAH	Marketing Authorization Holder
NDA	National Drug Authority
NPC	National Pharmacovigilance Centre
PBRER	Periodic Benefit-Risk Evaluation Report
PSRUR (PBRERS)	Periodic Safety Update Report
QPPV	Qualified Person for Pharmacovigilance
RMP	Risk Management Plan
SI	Statutory Instrument

1.4 Objectives of this guidelines

a) To specify the format and frequency of submission of safety update reports
b) To outline the points to note when preparing and submitting safety reports

1.5 Scope

This guideline applies to all drugs (human and veterinary) for which marketing authorization has been granted in Uganda.

1.6 Policy

These guidelines are drawn under section 3 (*Requirement for a pharmacovigilance system*) and section 4 *(Periodic safety update reports),* of the National Drug Policy and Authority (Pharmacovigilance) Regulations, 2014, Statutory instrument No.37.

1.7 Distribution

NDA website: *http://www.nda.or.ug*

A shared folder for all staff on NDA head office server (\\ndaserver\qms\guidelines);

PART 2: The Pharmacovigilance System

2.1 General

A licensed person shall have an appropriate system for pharmacovigilance and risk management in place in order to assure responsibility and liability with regards to the safety, efficacy and quality of their products on the Ugandan market.

A Marketing Authorisation Holder (MAH) should have in place local structures and processes for collection, collation, and reporting of ADRs and other safety and utilization data to NDA. The MAH shall be expected to leverage on the safety data from these local structures to facilitate preparation, quality control, review and submission of PSURs to with an impression of the Ugandan safety experience of the MAH`s product(s).

These structures and processes should be described by means of written policies and procedures in the marketing authorisation holder's (or their agents) quality system. The structures shall have capacity for case management of spontaneous and study reports, literature screening, signal management, additional pharmacovigilance and post-marketing research activities (for products with risk management plan (RMP) requirements), procedures for integration of information on benefits and risks from all available data sources.

2.2 Appointment of a Qualified Person for Pharmacovigilance and submission of PSURs

The licensed person shall appoint a designated Qualified Person for Pharmacovigilance, (QPPV), to be responsible for pharmacovigilance activities related to the drugs marketed in Uganda. The QPPV should be resident in Uganda, and have adequate theoretical and practical experience in pharmacovigilance. They should have medical training in pharmacy, pharmacology, clinical pharmacology or pharmaceutical sciences, with practical skills for the management of pharmacovigilance systems as well as expertise or have access to expertise in the pharmaceutical sciences, epidemiology and biostatics. A clear and demonstrable understanding of the local pharmacovigilance requirements shall be mandatory.

The QPPV will carry on the following responsibilities:

a) To establish a functional pharmacovigilance infrastructure and system capable of collecting safety information pertaining to the products marketed by the MAH. This

system should enable the MAH to effectively implement approved RMP(s) for products with risk management plan (RMP) requirements.

b) Submit to NDA, serious and non-serious reports of adverse reactions occurring in Uganda, related to the products marketed in Uganda on behalf of the MAH. The QPPV shall also notify the respective MAH of same, to facilitate incorporation of these reports as tabulations in the relevant PSUR section at the end of the reporting interval;

c) Being aware of and having sufficient authority over the content of RMPs applicable to marketed product

d) Submit PSURs prepared by the MAH to NDA, on the former's behalf;

e) Updating NDA on behalf of the MAH, of all other (besides ADR reports) safety data associated with the products that they have registered with NDA; and

f) Officially notify NDA of any significant safety issue(s) or regulatory action(s) taken by foreign agency or agencies, including the basis for such action(s) as per the timelines and provisions in this guideline.

g) Ensuring the necessary quality of data and reports submitted to NDA

2.3 Category of products for which PSURs are required

PSURs shall be submitted for all products on the Ugandan market, both generic and innovator. The NDA reserves the right to ask a marketing authorization holder to submit PSURs even for products out of this scope.

2.4 Format of the PSURs

The PSURS shall be presented in the format described in the EMA Guideline on good pharmacovigilance practices (GVP) Module VII – Periodic Safety Update Report (Rev 1) available online at:

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2013/04/WC500142468.pdf

and should be addressed to the Secretary to the Authority, National Drug Authority using standard cover letter (see format in Appendix 1).

2.5 Scope of the PSUR

The MAH shall prepare a single PSUR for all its medicinal products containing the same active substance with information covering all the authorised indications, route of administration, dosage forms and dosing regiments, irrespective of whether authorised under different names. There might be exceptional scenarios where the preparation of separate PSURs might be appropriate, for instance, in the event of different formulations

for entirely different indications. In this case, agreement should be obtained from NDA preferably at the time of authorisation.

2.6 PSURs for fixed dose combination products

In case of active pharmaceutical ingredients formulated as combination products but also marketed individually, information for the fixed combination may be reported either in a separate PSUR or included as separate presentations in the report for one of the individual substances. Listing related PSURs is considered important.

2.7 Periodicity and PSUR data lock point

NDA shall consider the product`s IBD to be the data lock point for inclusion of safety data in to the PSUR

Where an *ad hoc* ("for cause") report is requested and a PSUR has not been prepared for more than three years, a completely new report shall be prepared by the MAH.

2.8 Time interval between data lock point and the submission

The time interval between the data lock point and submission of PSURs shall be as follows:

a) PSURs covering intervals of 6 or 12 months: within 60 calendar days;
b) PSURs covering intervals in excess of 12 months: within 90 calendar days;
c) *Ad hoc* PSURs: 30 calendar days, unless otherwise specified in the *ad hoc* request.

2.9 Frequency of submission

The reports shall be submitted:

a) annually for a drug that has been manufactured, sold or supplied in Uganda, as the case may be, for less than ten years; but where new safety information regarded critical to the health of product users emerges, the MAH must inform the Authority immediately upon receipt of such critical information;

b) once every three years, for a drug that has been manufactured, sold or supplied in Uganda, as the case may be, for more than ten years but where new safety information regarded critical to the health of product users emerges, the MAH must inform the Authority immediately upon receipt of such critical information; and

c) any time, upon request by the Authority.

2.10 Reporting timelines for individual case reports

The following reporting timelines shall apply to valid individual case safety reports irrespective of the conditions of use of the suspected medicinal products:

a) all valid reports of serious and unexpected adverse events occurring in Uganda, within 24 to 48 hours of notification; and

b) all serious and expected, adverse event reports occurring in Uganda, reported as soon as possible but in any case not later than 15 calendar days.

c) all valid reports of serious and unexpected adverse events occurring outside Uganda, reported as soon as possible but in any case not later than 15 calendar days.

d) all non serious adverse event reports occurring in Uganda, reported within 90 calendar days

e) all serious expected adverse event reports occurring outside Uganda, a line listing covering a thirty day (30) reporting period should be submitted before the fifteenth (15) day of the next similar reporting period.

Note: For reports where only information regarding the suspected drug and suspected reaction are available, they should be submitted and follow up additional information submitted as soon as it becomes available.

2.11 Other field reports

The applicant shall submit to NDA the following information about the distributed drug products within five working days:

a. where a drug is suspected to be a counterfeit drug;

b. where a drug or its labeling is mistaken for another drug; and

c. any significant physical, chemical, therapeutic or any other change in the distributed product that renders the product unable to meet its established specifications at the time of marketing authorization.

Note: ICSRs and PSURs can be submitted via email at psur@nda.or.ug and an executive summary and covering letter submitted separately as per appendix 1.

2.12 Post-authorisation RMP update or new RMP

Drugs are registered by NDA on the basis that, when used in accordance with approved product information, their benefits outweigh their risks. As new information about the drug emerges during marketing experience, benefit-risk evaluation should be carried out to determine whether benefits continue to outweigh risks, and to consider whether measures need to be taken to improve the benefit-risk balance through risk minimization activities, e.g., labelling changes, communications with prescribers, or other similar measures.

Submission of RMPs shall therefore be necessary under the following circumstances:

a) Products for which RMPs were submitted at time of marketing authorisation, the MAH shall therefore be required to submit RMPs updates after 5 years post authorisation with the (first) 5-year renewal;

b) At the request of the Authority when there is a concern about a risk affecting the risk-benefit balance; and

c) With an application involving a change to an existing marketing authorization when the data included leads to a change in the list of the safety concerns, or when a new additional pharmacovigilance activity or a new risk minimisation activity is needed or is proposed to be removed.

2.13 Compliance with the pharmacovigilance provisions

The NDA will carry out, as deemed necessary pharmacovigilance audits to assess compliance with the pharmacovigilance reporting requirements specified in this guideline. These audits unless specifically communicated otherwise, shall assess compliance to the requirements of this guideline.

Appendix 1: Format for PSUR Covering Letter

To be printed on official company letter head paper

Date: .....

The Secretary to the Authority,
National Drug Authority,
Rumee Towers, Plot 19, Lumumba Avenue;
P.O. Box 23096,
Kampala, UGANDA.
Phone: (+256) 41-255665 / 347391/ 347392
E-mail: ndaug@nda.or.ug

Dear Sir/Madam

Subject: Submission of periodic safety update report

We are pleased to submit the periodic safety update report for the pharmaceutical product(s) whose details are as follows:

Name of the drug product……..
Dosage Form …… strength: ……
INN/active substance(s): ……
Reporting period: …… to …….

Attached herewith please find the report along with its printed executive summary prepared in the appropriate format as prescribed by the NDA "*Guidelines on submitting periodic safety update reports and any other reports that may be relevant to determine the safety, efficacy and quality of a drug*" document number DPS/GDL/034, on the following media:

- Printed executive summary
- An electronic copy

Yours sincerely,

Signature: ……

Name:……Designation/Title:……..……..

References

Guideline on good pharmacovigilance practices (GVP), Annex I –Definitions, 20 February 2012, EMA/876333/2011.

Guideline on good pharmacovigilance practices (GVP), Module V – Risk management systems (28 March 2017 EMA/838713/2011 Rev 2).

Guideline on good pharmacovigilance practices (GVP), Module VII – Periodic Safety Update Reports. (19 April 2013 2 EMA/816292/2011 Rev 1)

International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use; ICH harmonised; tripartite guideline periodic for benefit-risk evaluation report (PSUR) E2C (R2).

National Drug Policy and Authority (Pharmacovigilance) Regulations No. 37, of 2014.

Document Revision History

Date of revision	Revision number	Document Number	Author(s)	Changes made and/or reasons for revision
12 April 2018	0	DPS/GDL/034	*Author:* Julius Mayengo *Reviewers:* *Helen Ndagije* *Victoria Nambasa* *Evans Tusubiira* *Jeanne Muhindo* *Peter Ssali*	This is the first issue of this document

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