

Pharmacovigilance-A Master Key for Drug Safety

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Abstract:

Pharmacovigilance is emerging widely in this competitive world. It can be considered as a major factor which can help in minimizing the cause of diseases. This can help in minimizing the cause of diseases. This can reach to the public and can create an huge awareness within them to address the report of ADR .By involvement of people it can be reduced. Pharmacovigilance can also know as drug safety monitoring place. It plays a significant role in the clinical research. The main aim is to protect the public health by assuring the drug safety. Even though there will be a number of consequences, risk factors arise, by overcoming those parts by the active involvement of the people. In this review it has been clearly discussed about the factors affecting ADR and how people can access through their forms.

Key Words: Pharmacovigilance, Drug safety, ADR Reporting

INTRODUCTION:

Pharmacovigilance also known as drug safety or tranquilize wellbeing and that is the science which deals with the discovery, assessment, knowing about the understanding, prevention and also the addressing of the adverse drug reaction. Pharmacovigilance mainly concentrates on improper medications responses which have been analyzed based on the noxious and pretended symptoms. Basically pharmacovigilance is word derived from a Greek and latin explaining as PHARMAKON a greek word which refers as “drug” and the VIGILANCE a latin word which refers as “to watch”.^[1]

Scope of pharmacovigilance:

The principle of pharmacovigilance was considered early from 1972 WHO technical support and stays a energetic, clinical and experimental principle. It has been set important to meet the consequences of wider range and potency of pharmaceutical and biological medicines including vaccines. When adverse effects and noxious appear, it is important that they are interpreted and interacted effectively to the public that has the observation to analyze the information. To satisfy the pharmacovigilance contract for its marketed products as per regulations.^[2]

Inception of clinical trials in India:

In the year 2005 the global pharmaceutical companies have established the clinical trials setup in India for the research purposes.^[3]

Advantages of conducting clinical trials in India

Clinical trials in India provide a high degree of conformity to international guidelines such as ICH-GCP and regulations as followed by US-FDA. This includes

1. Opportunity of experienced English speaking R&D professionals including medical practitioners.
2. Continuing guide and collaboration from government sector
3. Less expensive when compared to other countries.^[4]

SWOT analysis in clinical trial section:

Strengths:

1. Third biggest member in the world with 500 API's^[5]
2. Conformity with GCP- standards^[6]
3. Arising developmental governmental policies^[7]
4. Large data drilling related to safety profile of drug possibilities due to heavy population.^[8]

Weakness:

As per 2009 -10 an approximate investment on health and medical sector is about 2.1% of total amount.

Developed countries like US, France and Germany have spent around 165.11%, 10.8%, 10.4% of GDP respectively^[9].

Opportunities:

The Indian community is the biggest source of human biodiversity. Intelligent possible for skilled human resources required for an effective pharmacovigilance system.^[10]

Threats:

- Under-describing of Adverse Drug Reactions
- Low opportunity of funds
- Less ADR's monitoring centers.

Patient report to pharmacovigilance system:

The Pharmacovigilance systems are emerging towards the people's friendly network in order to report the Adverse Drug Reactions

Methods of systematic review:

A systematic review was conducted to the patient reporting the ADR. The studies were revealed on the

- ✓ Review about patient describing
- ✓ Examination of those patients reports according to national (or) super national authorities.
- ✓ Analogy was done between the patient and healthcare professional reports given to pharmacovigilance authorities.
- ✓ Analysis of patient experiences, suggestions and awareness about reporting ADR's.

As per this study a total number of 34 studies were conducted in which, out of these 34 studies, they have been divided as

- 5 - Study based on review
- 14 - Retrospective observational studies
- 9 - Collection of surveys
- 6 - Studies on mixed research methods.

And the findings from the study of patient reporting states that:

- a) Patient describing suggests advanced information's
- b) Helps in better answerable process in the regulatory activities^[11]

Factors affecting the ADR reporting:

This was concluded by a study conducted in between 133 healthcare professionals comprising medical doctors, pharmacists, health officers and nurses. Some of the drawbacks or factors have been identified, and they have classified accordingly as discouraging factors and encouraging factors.^[12]

- a) Discouraging factors:
 - i) Lack of knowledge & consciousness on what, when and whom to report.
 - ii) Improper format
 - iii) Problem with the following procedures
 - iv) Blind (or) absence of authorized body.
 - v) Lack of commitment of healthcare professionals.
- b) Encouraging factors:
 - i) Consciousness on what when at all levels of education
 - ii) On-service training
 - iii) Regularity check of patients^[12]

Future of Pharmacovigilance:

There are some certain considerations of pharmacovigilance in future.

- a) Pharmacovigilance should consider the negative comments at least level and should enhance the awareness of safety towards public.
- b) Complicated risk- benefits decisions are responsible and likely to increase the use of formal-decision analysis
- c) Pharmacovigilance should be made aware in a culture of scientific development. It needs a proper and right supports from various preparations, a good academic base and wider availability of training and resources.
- d) Systematic analysis of pharmacovigilance process and the results should be enhanced and performed based on the standards level.^[13]

Challenges of pharmacovigilance:

- i) Globalization
- ii) Web-based sales and information
- iii) Broader safety concerns
- iv) Monitoring of established products.
- v) Orthodox bias in drug research,
- vi) larger gaps between guidelines and laws
- vii) Poor knowledge of medical professionals in drug administration

viii) Lacking experienced resources in pharmacovigilance^[14]

Pharmacovigilance program in India (PVPI):

PVPI was initiated and introduced by the Indian regulatory authority (Central Drug Control Standard Organization). Ministry of Health and family welfare under DCGI under CDSCO started with an aim to protect the public health safety. This is working under the steering committee. The members of the steering committee includes

- Member secretary (Assistant drug controller, New Delhi, India)
- Director, AIIMS (ex-officio)
- DCGI(ex-officio)
- Head of department of pharmacology, AIIMS (ex-officio)
- Scientific director of Indian Pharmacopoeial commission (ex-officio)
- Nominee of director general, ICMR, (ex-officio)
- Nominee of vice-chancellor medical/pharmacy university (ex-officio)

It was started by government of India in July 14 2010 in collaboration with All India Institute of Medical Sciences [AIIMS]. 22 Adverse Drug monitoring centers have been started under this programme.

Any drug to be marketed must have undergone clinical trials in order to prove its safety and efficacy. During this trial or after the completion of trials there may be chances of occurrence of adverse reactions, in order to monitor those adverse reactions after the marketing pharmacovigilance is essential.

Mission of PVPI:

To safeguard the health of Indian population by ensuring that the benefits of use of medicine outweigh the risks associated with its use.

Vision of PVPI:

To improve the patient safety and welfare in Indian population by monitoring the drug safety and thereby reducing the risks associated with the use of medicine.

Objectives of PVPI:

- i) To develop a national-wide system for patient safety monitoring
- ii) To determine and examine the new signal (ADR) from the reported cases
- iii) Examine benefit-risk ratio of marketed medications
- iv) Accomplish the evidence based information on safety of medicine.
- v) Arise as a national center of excellence for pharmacovigilance activities
- vi) Helps in providing training and consultancy support to the other pharmacovigilance centers.^[15]

PVPI phases:

PVPI is a 5 year programme and it consists of totally 5 phases..

- a) Initial phase
- b) Expansion and consolidation phase
- c) Expansion and maintenance phase

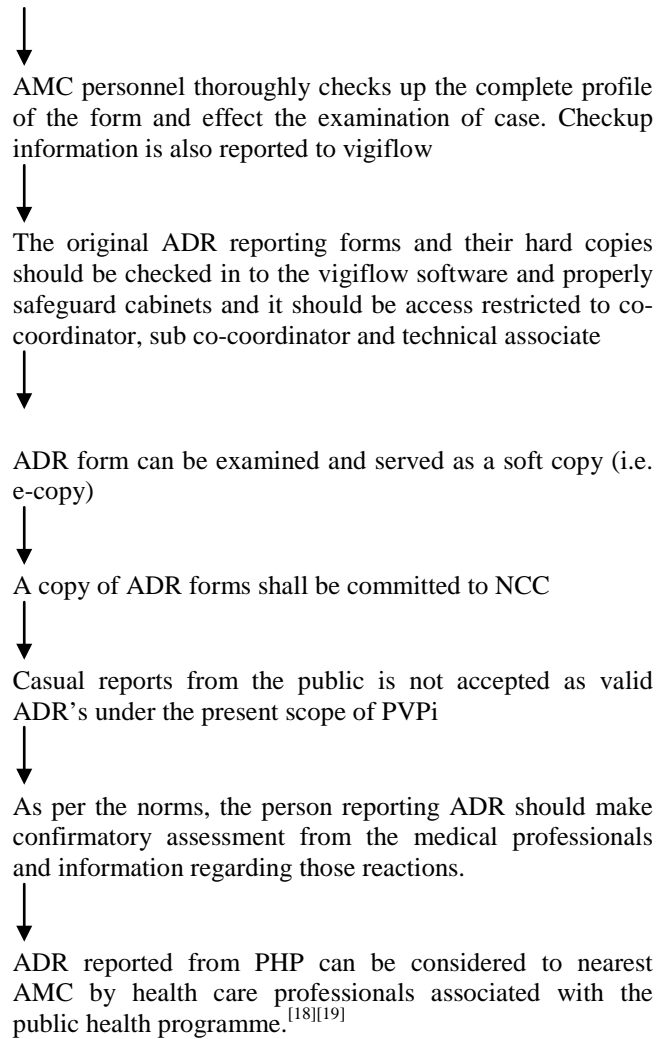
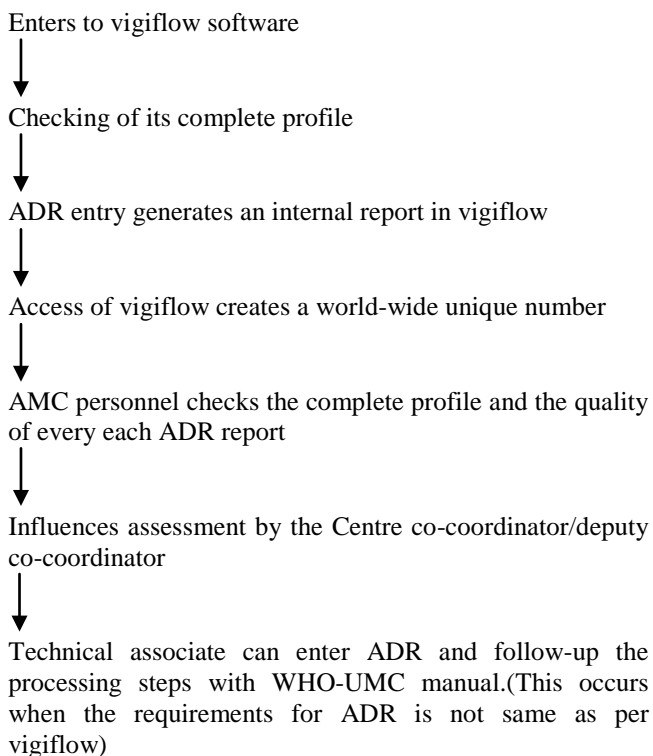
- d) Expansion and optimization phase.
 - e) The Excellence phase.
 - a) Initial Phase:
 - Developing systems and procedure
 - Enrollment of 40 medical institute
 - Start data collection from AEFI
 - b) Expansion and consolidation phase:
 - Linkage with UMC, Sweden
 - Identify gaps and address via proper training
 - Training of PV software supply by UMC, WHO
 - c) Expansion and maintenance phase:
 - Enrollment of additional hundred medical institute
 - Software development and validation
 - Zonal workshop of drug safety public awareness.
 - d) Expansion and optimization phase:
 - Training of PV human resources
 - Newsletter publication of drug safety
 - Create center of excellence for PV in Asia pacific
- PVPi is governing totally 2 zonal, 5 regional and 24 peripheral regions.^{[16][17]}

Reporting procedure in India:

The reporting of pharmacovigilance in India is done in three ways

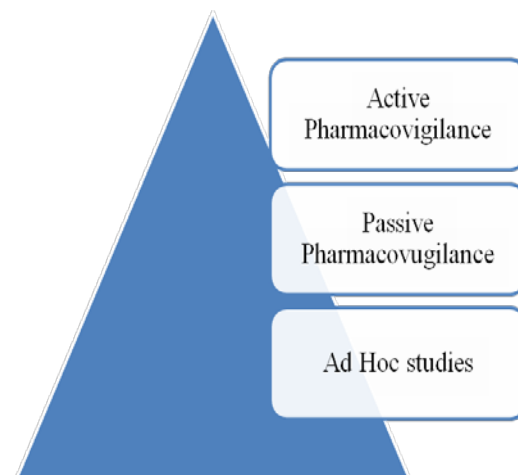
- a) Health care professional
- b) Public reporting (i.e. consumers)
- c) Public health programme-PHP

These reports are documented by reporting in a ADR reporting form which is issued and managed by ADR monitoring center/National co-ordination center.



Pharmacovigilance methods:

There are 3 methods in the pharmacovigilance. Such as:



1) Passive surveillance

- It encloses all casual AEFI reporting
- From vaccine services providers and hospitalized patients.
- Reach next levels

2) Active surveillance:

- Mainly used for the design of AEFI profile, rates and risk factors
- Procedural and capability constraints limit wide application.
- Can also be executed in the community setting.

3) Ad Hoc studies:

- Epidemiological studies eg: Cohort study, case-control study, case series studies)
- Target on selected immunization
- Retrospective or prospective^[20]

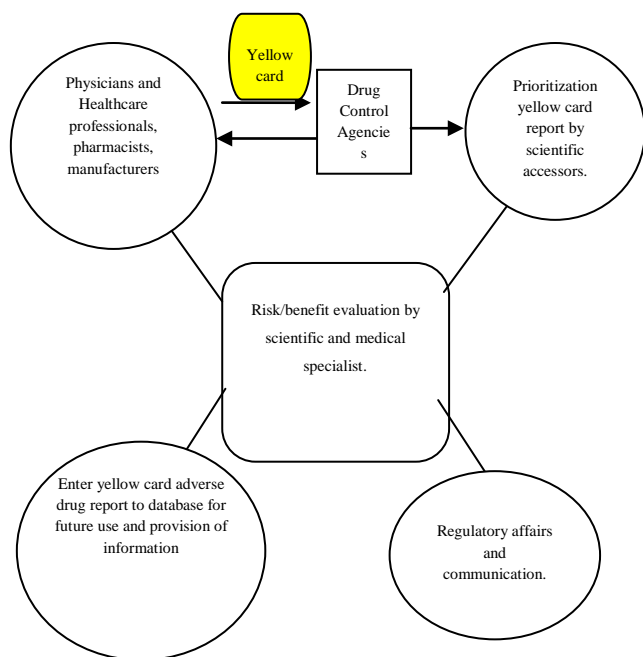
Pharmacovigilance and International health:

The present world-wide network of pharmacovigilance is monitored by the “UPPSALA MONITORING CENTRE”, and it will be reinforced by a separate system of review. This can be considered as an antagonistic and critical drug safety concern that has the capability to affect the public health conflicting beyond national boundaries.

The difficulty of ADRs on public health against the progress in pharmacovigilance has difficult on public health of ADR’s remains important^[21]. Pharmacoeconomic studies on the charge of the adverse reaction gives idea that governments pay some appreciable charges from the health budgets towards the covering amounts associated with them.^[22]

Yellow card-Scheme for ADR reporting:

Yellow card scheme were applied to some of the ADR reporting system. This system was established in 1964 as a outcome of thalidomide tragedy. After sometime this system has become one of the important international pharmacovigilance services.^[23] The yellow card have been segregated into different priorities by a scientific member according to the drugs.



The yellow card scheme is developed by the medicine control agency and committee on safety of medicines. This scheme has been supported by a new monitoring system called ADROIT (Adverse Drug Reaction Online Tracking system). This system helps in scanning the yellow card image through optical system and helps in saving the data. This also helps in identifying the early detection of ADR.^[24]

Starting of a pharmacovigilance center:

A pharmacovigilance system has now started emerging in order to address the adverse events. Since it is a new beginning, it requires some time to develop their vision, expertise and continuity. It can be initiated by starting a small centre in one hospital and can be followed up by a chain process in other nearby hospitals. This centre can be initiated by expertise in pharmacology, clinical toxicology, clinical pharmacy, pharmacy practice and academicians. But in order to attain its position a governmental department can be as a good backbone supporter to step-up a pharmacovigilance centre.

Requirements for setting a pharmacovigilance centre:

- Make a exposure with the health authorities and with local, zonal or international institutions and groups employed in a clinical medicine, pharmacology and toxicology explaining the significance of the project and its purposes.
- Plan a reporting form and begin to gather the data by allocating it to hospital departments, family practitioners etc.,
- Manufacture a copy to inform the health professionals about definitions, aims and methods of the pharmacovigilance system.
- Generate the centre: Staff, workers, accommodation, telephone, word processor, database management capability, bibliography.
- Look after of the education of pharmacovigilance staff with regard:
 - Data gathering and confirmation
 - Explaining and coding of adverse reaction representation
 - Coding of drugs.
 - Case evaluation assessment
 - Signal observation
 - Risk management
 - Set up a database
 - Conduct the meetings in hospitals, academia and professional institutions, describing the principle and request of pharmacovigilance and the significance of reporting.
 - Upgrade the consequences of describing the adverse drug reactions through medical journals, other professional publications and communication activities.
 - Keep up the exposure with international institutions working in pharmacovigilance.

ADR reporting process:

This ADR reporting process can be done in 3 steps to find the better outcome and to prevent the occurrence of adverse drug reactions

- a) What to report?
- b) Where to report?
- c) Whom to meet?

a) What to report:

PVPi motivate and supports all types of expected ADR's reporting whether they are recognized, non-recognized, significant, non-significant, recurring or often recurring regardless of an accepted apathetic relationship between a drug and the reaction. ADR's with the usage of allopathic medicines, Vaccines, traditional medicines, medical devices, contrast media etc are to be announced.

b) Where to report:

All healthcare professionals (clinicians, dentists, pharmacists, nurses) patients/ consumers can analyze the ADR's to NCC or AMC's. The pharmaceutical companies can also send a separate case safety reports for their product to NCC.

c) How to report:

In order to report ADR, Suspected ADR forms are available on the IPC websites; people can access through the ADR forms and can submit their reports. The reporting forms are available in 10 different languages such as Tamil, Telugu, Kannada, Bengali, Gujarati, Assamese, Marathi, Oriya, and Malayalam. For further submission they can also submit their views through a helpline number (18001803024) from 9.00am to 5.30pm.^[25]

d) Who to report:

The patients who have submitted their forms either directly to NCC or through AMC are those reports can be evaluated by the expertise in AMC and forward those reports into vigiflow database for further justification^[26]. Then these reports are sent to NCC and then to WHO-UMC the information obtained from the patients through the assessment may help the exports to develop new signals to prevent forthcoming indications.^[27]

Different concerns in reporting:

- a) Whether reporting can be centralized (or) regional wise:

The aim of setting up a pharmacovigilance a national- wide is to obtain a common overview from the public. But on an average statistics it was found that the number and quality of ADR reporting was more in region wise then nationally. So it is better to begin with region wise data collection and can then forward to national wise. A small limitation in setting up a region wise reporting requires more staff as well as too expensive.

- b) Stimulation of reporting:

The ADR reporting requires a frequent refreshment to develop good positive comments over the pharmacovigilance, to strengthen this system. The changes can be done in the following.

- Simple way to handle the reporting forms.
- Accepting the receipt of ADR either through personal letter or phone call.

- Assuring the people in relating their feedbacks with articles and journals
- Encouraging the staff to participate in PG education and scientific meetings.
- Co-operation with professional union

- c) Progress under-reporting of ADR:

The reporting of ADR is a common progress. Changes to this process is difficult, because patients reporting in the forms are very less whereas in WHO monitoring centre they receive 200 adverse event per year, so as to develop this system. The importance of meeting, simple procedures for reporting and good motivational practice may be noted to avoid the issues in reporting ADR.

Practicalities in the administration of the pharmacovigilance centre:

The most important thing in organizing a centre is staff.

- a) Staff: The staff of the pharmacovigilance centre can be from different disciplines such as:

- Clinical medicine
- Pharmacology
- Toxicology and epidemiology

But it is very rare to set up a pharmacovigilance centre by a part-time physician and a pharmacist.

- b) Necessary equipment:

Some of the useful equipment should be there to start a pharmacovigilance centre. They include:

- Multi-connection telephone
- Computer
- Printer
- Fax
- e-mail
- photocopier

- c) Continuity:

It is mandatory to have a secretariat to continuously access the service reporting the adverse events by monitoring phone calls, mails, maintenance of the database, literature documentation, co-ordination of activities.

- d) Advisory committee:

There should be a designed advisory committee to help and support the pharmacovigilance centre to access the

- data collection
- interpretation of data

This committee may involve the members from the following disciplines:

- General medicine
- Pharmaceutics
- Clinical pharmacology
- Toxicology
- Epidemiology
- Pathology
- Drug regulation and quality assurance
- Drug information
- Phytotherapy

- e) Information service:

The major requirement of pharmacovigilance system is to provide sufficient information in relative with assessment

case report. To provide this information they require a literature information area and also a well-established library within reach.

National pharmacovigilance centre has a non-line approach to the database of the UMC and be on the mailing list of the adverse drug reaction and the drug newsletter produced by the world health organization and many national wide or regional centers all over the world.

f) Communications

A newsletter is circulated to healthcare professionals in order to discuss the information and updates in the medical field. This may help to minimize the ADR's.

g) Poison control and drug information centre:

Poison control and drug information centers have much in normal with the pharmacovigilance centers, both in the administration and from a technical point of view. If pharmacovigilance is begin in a country where a poison control or drug information centre is already in a position it may be strong enough to develop the pharmacovigilance system in coincidence with it.

Evaluation of case reports:

The evaluation of adverse drug reaction case reports requires a expertise in assessing the forms in that expertise may be of from different disciplines such as clinical medicine, pharmacology, toxicology and epidemiology. This expertise may be increased by training the staffs by the special consultants.

i) Quality of Documentation:

Entire details and analyzing of data, quality of interpretation, keep up-dating.

ii) Coding:

Drug names should be entered in a organized way. For coding of the adverse events the WHO Adverse Reaction Terminology (WHOART) or any other internationally recognized expression (e.g.: medDRA) should be used.

iii) Relevance:

Whenever there is an identification of new symptom or identifications with relevant to new drugs. To clarify these indications, some of the questions can be listed, such as

a) Whether it is new drug?

The drug is considered as new drug when the pharmaceutical product in the market is less than five years.

b) Whether it is a unknown reaction?

When they have mentioned in summary of product characteristics, (or) whether the particular reaction has been described in the literature

iv) Identification of duplicate reports:

Certain essential quality of a case (sex, age or date of birth, dates of drug exposure etc.) may be used to find out the duplicate reporting.

v) Causality assessment or imputation:

With some deviations, case reports explain predicted adverse drug reactions. Different approaches have been developed for the complex resolution of likelihood of a causal connection between the drug exposure and adverse events.

- The federation in time between drug administration/event
- Pharmacology
- Medical or pharmacological reasonable

Use of the data:

a) Hypothesis generation and strengthening:

A major focus on pharmacovigilance is the prior interpretation of hypothesis or signals with consideration to feasible adverse reaction. Prior signals may be too unknown however to explanation firm for conclusions and regulatory actions and may need further study. Therefore international co-operation is very important.

b) Drug regulation:

If a drug has been approved in a market, it requires a continuous monitoring by the regulatory agency (or) pharmaceutical company. The problems can be overcome by adjusting the information of the product.

Relationship with other parties:

- i. Drug regulatory authority in the country requires to be enlightened about expected adverse reactions without being late, especially when it is not usual. The pharmacovigilance centre should tell the regulatory authority about any clump of case reports, when an adverse reaction has been described in a greater frequency.
- ii. The information about the drug product is same as required by regulatory authority as well as pharmaceutical company. It depends on the information whether it should be informed to regulatory agency (or) directly to the company.
- iii. A pharmacovigilance team takes the support from medical and pharmaceutical associations to help the public.

Funding:

A certain amount has been required for setting up of a pharmacovigilance centre based upon the amount of population. This centre should have some common continuous source of collecting in order to make sure the continuity in its work. Beside from common resources the centre may require extra funding from various agencies with a interest in pharmacovigilance such as:

- ❖ Health insurance companies and health insurance funds.
- ❖ University apartments
- ❖ Professional associations
- ❖ Governmental departments with an interest in drug safety.^[28]

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by healthcare professionals

CDSCO Central Drugs Standard Control Organization Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, FDA Bhavan, ITO, Kotla Road, New Delhi www.cdsc0.nic.in					(AMC/ NCC Use only) AMC Report No. _____ Worldwide Unique no. _____					
A. Patient Information					12. Relevant tests / laboratory data with dates					
1. Patient Initials _____		2. Age at time of Event or date of birth _____		3. Sex <input type="checkbox"/> M <input type="checkbox"/> F		4. Weight ____ Kgs				
B. Suspected Adverse Reaction					13. Other relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/ renal dysfunction etc)					
5. Date of reaction stated (dd/mm/yyyy)					14. Seriousness of the reaction <input type="checkbox"/> Death (dd/mm/yyyy) _____ <input type="checkbox"/> Life threatening <input type="checkbox"/> Hospitalization-initial or prolonged <input type="checkbox"/> Disability <input type="checkbox"/> Congenital anomaly <input type="checkbox"/> Required intervention to prevent permanent impairment / damage <input type="checkbox"/> Other (specify) _____					
6. Date of recovery (dd/mm/yyyy)										
7. Describe reaction or problem										
					15. Outcomes <input type="checkbox"/> Fatal <input type="checkbox"/> Recovering <input type="checkbox"/> Unknown <input type="checkbox"/> Continuing <input type="checkbox"/> Recovered <input type="checkbox"/> Other (specify) _____					
C. Suspected medication(s)										
S.No	8. Name (brand and /or generic name)	Manufacturer (if known)	Batch No./ Lot No. (if known)	Exp. Date (if known)	Dose used	Route used	Frequency	Therapy dates (if known give duration)		Reason for use of prescribed for
								Date started	Date stopped	
i.										
ii.										
iii.										
iv.										
Sl.No As per C	9. Reaction abated after drug stopped or dose reduced					10. Reaction reappeared after reintroduction				
	Yes	No	Unknown	NA	Reduced dose	Yes	No	Unknown	NA	If reintroduced dose
i.										
ii.										
iii.										
iv.										
11. Concomitant medical product including self medication and herbal remedies with therapy dates (exclude those used to treat reaction)							D. Reporter (see confidentiality section in first page)			
							16. Name and Professional Address : _____			
							Pin code : _____ E-mail _____			
							Tel. No. (with STD code): _____ Occupation _____ Signature _____			
							17. Causality Assessment		18. Date of this report (dd/mm/yyyy)	

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CONCLUSION:

As the pharmaceutical companies are going at a very fast rate in their growth in regarding their new invention of medications for the emerging diseases so it is important to note down the side effects caused by the medications parallel and have to take a remedy for the serious adverse reactions. Now the pharmacovigilance has been made a user-friendly network for reporting the adverse events. Hence by measuring these adverse reactions we can make a alternate solutions in order to overcome the adverse events and hence it can be recovered. By assessing the reporting forms of adverse drug reactions it helps in better development and implementing of newer systems in regulating the pharmacovigilance. This system can acts a preventive cause for further development of new adverse reactions. People can use this platform to record their ADR's which can be maintained as confidential and the feedback or remedy for the reported ADR can be given with the suspected time. It can also be very useful to the healthcare professionals, regulatory authorities, pharmaceutical companies and also consumers to monitor the risk of medicines. Even though there is a PVPi programme it helps only in reporting but on continuous follow of this source can helps in a unique regulation for pharmacovigilance in India.

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