**Pharmacovigilance**

Pharmacovigilance is the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term side effects of medicines. Pharmacovigilance is the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications, biologicals, herbalism and traditional medicines with a view to:

* Identifying new information about hazards associated with medicines
* Preventing harm to the patients.

Pharmacovigilance starts from the clinical stage and continues throughout the product life cycle of the drug, mainly divided as Pharmacovigilance during **pre-marketing** (that is clinical phase) and **post-marketing**. The process of collection of such information about a drug begins in phase I of the clinical trial, before approval of the drug, and continues even after approval; several post-market safety studies are conducted, with many made mandatory by drug regulatory agencies around the world.

The Pharmacovigilance effort in the India is coordinated by The Indian Pharmacopoeia Commission and conducted by the Central Drugs Standard Control Organization (CDSCO).

**Why Pharmacovigilance in India?**

The information collected during the pre-marketing phase of a medical drug is inevitably incomplete with regard to possible adverse reactions:

1. Tests in animals are insufficiently predictive of human safety

2. Patients in clinical trials are selected and limited in number, the conditions of use differ from those in clinical practice and the duration of trials is limited.

3. Information about rare but serious adverse reactions, chronic toxicity, and use in special groups (such as children, the elderly or pregnant women) or drug interactions is often incomplete or not available.

**Major aims of Pharmacovigilance**

Pharmacovigilance is concerned with the detection, assessment and prevention of adverse reactions to drugs. Major aims of pharmacovigilance are:

1. Early detection of adverse reactions and interactions

2. Detection of increases in frequency of (known) adverse reactions

3. Identification of risk factors and possible mechanisms underlying adverse reactions

4. Estimation of quantitative aspects of benefit/risk analysis and dissemination of information needed to improve drug prescribing and regulation.

**Risk Benefit**

The term ‘benefit-risk ratio’ is often used as a general term linked to the use of a medicine. To balance risk and benefit is, however, a very complex exercise. Usually the risks of a medicine are of a totally different nature and frequency compared with its benefits. For most medicines the benefits are limited to a few indications and for an individual patient there is usually only a single benefit sought but the potential risks are multiple.

For newer medicines, where there is likely to be limited experience, conservative estimates of the overall merit seem preferable so that the prescriber will use the drug critically. Subsequently, re-evaluation of the risk -to-benefit balance is necessary as greater knowledge of efficacy and adverse effects is acquired.

**Severity Vs Seriousness**

The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a patient's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

**Causality**

Causality (also referred to as causation) is the relationship between an event (the cause) and a second event (the effect), where the second event is understood as a consequence of the first. In common usage, causality is also the relationship between a set of factors (causes) and a phenomenon (the effect). Anything that affects an effect is a factor of that effect.

**Why causality assessment?**

An inherent problem in pharmacovigilance is that most case reports concern suspected adverse drug reactions. Adverse reactions are rarely specific for the drug, diagnostic tests are usually absent and a rechallenge is rarely ethically justified. In practice few adverse reactions are ‘certain’ or ‘unlikely’; most are somewhere in between these extremes, i.e. ‘Possible’ or ‘Probable’. In an attempt to solve this problem many systems have been developed for a structured and harmonised assessment of causality. None of these systems, however, have been shown to produce a precise and reliable quantitative estimation of relationship likelihood. Nevertheless, causality assessment has become a common routine procedure in pharmacovigilance.

**The WHO-Uppsala Monitoring Centre (WHO-UMC) causality assessment system**

The WHO-UMC system has been developed in consultation with the National Centres participating in the Programme for International Drug Monitoring and is meant as a practical tool for the assessment of case reports. It is basically a combined assessment taking into account the clinical-pharmacological aspects of the case history and the quality of the documentation of the observation.

**Expectedness**

The WHO defines as Expectedness of an AE/ADR may be product or product use specific, and separate investigators brochures may be used accordingly in different clinical trials. However, such documents should cover all information on ADRs that applies to all affected product presentations and uses. When relevant, separate discussions of pertinent product – specific or use specific safety information in clinical trials, should also be included in the investigators brochures.

Any ADR occurring in a clinical trials that qualifies for special attention and is observed with, one product dosage form or use should be cross – referenced in the investigators brochures for all dosage forms and uses during the clinical development of an investigational medicinal product.

**Outcome of Adverse Event**

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 and the outcome of Adverse Event described the conditions as follows:

Fatal- fatal describes conditions, circumstances, or events that have caused or are destined to cause death or dire consequences: a fatal illness.

Continuing- continuing describes the condition when the treatment is going on

Recovering- Return to a normal state of health, mind, or strength

Recovered- the patient appears cured from illness or disease.

Unknown- Unknown describes the condition when the result is not known

**Methods of /Sources of Report in PVG**

The basic principles that underlie most systems are considered ill the following sections.

***1. Individual reporting***

Doctors are the major source of reports. Those whose practice is primarily outside hospitals tend to care for patients for prolonged periods of time and may therefore also see the occurrence of slowly developing or delayed reactions. Since most severe reactions are seen in hospitals, physicians who are hospital-based are often able to ascertain previous drug administration, link it to the reaction, and submit a report.

The physician, during an outpatient or inpatient examination, may decide that the patient has a recognizable syndrome of signs, symptoms, and/or laboratory findings and that this syndrome may be associated with a previously administered drug. He / She then report this information to the centre.

***2. Comprehensive monitoring***

Comprehensive monitoring is typically performed in a hospital setting and the input consists of abstracts of patient identification, drug administration, and patient reactions. Specialized methods are used to ensure that this information is complete, and case reports or tabulated summary data can be supplied to the national centre.

**3. Population monitoring**

In population monitoring the records of hospital or clinic patients, or of the entire population of a district, may be employed. Such monitoring could be effective when a large stable population is surveyed in an organized medical care system.·As rapid advances are being made in the electronic processing of patient documentation and records, there may be unusual opportunities to incorporate a drug monitoring element in these systems.

Population monitoring appears to have much to offer in that actual rates of reactions being obtained and truly unexpected reactions may be identified. It is complex and expensive, however, and the patient population may not be large enough for the detection of rare (1 in 10 000-50 000) reactions. This system would automatically record drug use and patient syndromes or events, permitting searches for associations between the two. The results of such searches may be reported to the national centre.

***4. Other sources***

All potential sources of information should be considered. Each national centre must seize opportunities to exploit old and develop new sources of information. For example, useful information can come from poison control centres, social security records, inquest reports, and from clinical and basic pharmacology, toxicology, and pathology units.

**Valid Report**

The Individual Case Safety Report (ICSR) is a standard for the capture of the information needed to support the reporting of adverse events, product problems or consumer complaints associated with the use of FDA regulated products or a report received by a company or agency which describes an adverse event.

Reports, describing serious adverse drug reactions that needed to be exchanged in pharmacovigilance between the various parties in accordance with community legislation, are referred to as ICSRs or safety reports.

The minimum information needed for a Valid Report according to ICH E2B is:-

a. One identifiable patient

b. Identifiable reporter

c. One reaction / event &

d. One suspected Drug

**Periodic safety update reports (PSURs)**

Periodic safety update reports (PSURs) are pharmacovigilance documents intended to provide an evaluation of the risk-benefit balance of a medicinal product for submission by marketing authorisation holders at defined time points during the post-authorisation phase.

The main objective of a PSUR is to present a comprehensive and critical analysis of the risk benefit balance of the medicinal product taking into account new or emerging information, in the context of cumulative information, on risks and benefits. The PSUR is therefore a tool for post-authorisation evaluation at defined time points in the lifecycle of the product.

**Medication Errors**

Medication errors are mishaps that occur during prescribing, transcribing, dispensing, administering, adherence, or monitoring a drug. Examples of medication errors include misreading or miswriting a prescription. Medication errors that are stopped before harm can occur are sometimes called “near misses” or “close calls” or more formally, a potential adverse drug event. Not all prescribing errors lead to adverse outcomes. Some do not cause harm, while others are caught before harm can occur (“near-misses”). Medication errors are more common than adverse drug events, but result in harm less than 1% of the time. About 25% of adverse drug events are due to medication errors.