# PHARMACOVIGILANCE: SCOPE FOR A DERMATOLOGIST

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**Abstract**

Pharmacovigilance is defined as the science of detection, assessment, and prevention of adverse drug reactions in humans. Under-reporting of drug reactions is the major problem and has various reasons. The WHO has initiated the program of reporting all adverse drug reactions now co-ordinated by the Uppsala Monitoring Centre in Uppsala, Sweden, with oversight by an international board. This article presents in brief the relevance, functioning, importance, and the procedure of reporting adverse drug reactions. Dermatologists have the greatest opportunity in reporting various reactions that can happen as they come across majority of these drug reactions, prescribed by all sectors of the health system.

**Key Words:** *Adverse drug reactions, drugs, pharmacovigilance*

## Introduction

We are all aware of the great thalidomide tragedy that occurred in early 1960s. Thalidomide was considered to be one of the greatest discoveries of those days. It was used in a myriad of conditions and in Germany, when pregnant woman complained of sleeplessness, thalidomide was prescribed. Subsequently many thousands of congenitally deformed infants were born as a result of exposure in-utero to an unsafe medicine. This forced the sixteenth World Health Assembly to adopt a resolution (WHA 16.36)[1] that reaffirmed the need for early action in regard to rapid dissemination of information on adverse drug reactions and led, later to creation of the WHO pilot research project for International Drug Monitoring in 1968.

From these beginnings emerged the practice and science of pharmacovigilance, defined as the science of detection, assessment, and prevention of adverse drug reactions (ADRs) in humans.[2]

The pilot project has developed into the WHO Program for International Drug Monitoring now co-ordinated by the Uppsala Monitoring Centre (UMC) in Uppsala, Sweden, with oversight by an international board.

The program has expanded to include over 108 countries. In many countries, regional reporting centers, interest groups, dedicated internal medicine, and pharmacology department units' drug and poison information centers and other non-governmental organizations have developed to report the ADRs. By July 2008, over 4 million cases were recorded. However, this figure represents only the tip of an iceberg.

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The situation is India is very poor as far as the reporting of ADRs is considered. The nodal centre is situated in AIIMS, New Delhi. The program functioning has not been able to achieve the desired results. Many regional and zonal centers have yet to take shape.

Under-reporting of drug reactions is the major problem; reasons include lack of time and report forms, and the misconception that absolute confidence in the diagnosis of an adverse reaction is important.[3]

## Relevance of Pharmacovigilance

Before a product is marketed commercially, it goes through various phases of clinical trial to establish its safety and efficacy before its use in day-to-day practice. However, the clinical trials done have many limitations:

- Strict criteria of inclusion and exclusion make it to be used in a very selective group of "otherwise normal patients." This is not so in our day-to-day practice as most of our patients would be having many other co-morbidities or on certain drugs already.
- Special groups such as children, pregnant woman, or old age population are not studied during the trials.
- Other factors causing drug reactions such as genetic factors, environmental factors, drug–drug interactions, drug–virus interactions, drug–disease interactions etc. may not have been studied during the clinical trials.
- Rarer reactions or chronic toxicities may not be detected until a very large number of patients are studied. For example, if a drug has a chance of causing serious

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drug induced hepatitis in 1 in 10,000 population, then a minimum of at least 30,000 people need to be treated to detect such a reaction.[4]
- Tests in animals are insufficient to predict human safety.

## The Purpose of Pharmacovigilance

Phamacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems. Recently, its concerns have been widened to include:[5-8]
- Herbals
- Traditional and complementary medicines
- Blood products
- Biologicals
- Medical devices, and
- Vaccines.

The specific aims of pharmacovigilance are to:
- Improve patient care and safety in relation to the use of medicines and all medical and paramedical intervention
- Improve public health and safety in relation to the use of medicines
- Contribute to the assessment of benefit, harm, effectiveness, and risk of medicines, encouraging their safe, rational and more effective (including cost-effective) use and
- Promote understanding, education, and clinical training of pharmacovigilance and its effective communication to the public.[9]

## Functioning of Pharmacovigilance

The headquarters of the WHO program is situated in Uppsala, Sweden and is co-ordinated by the Uppsala Monitoring Centre.[10] The principal function of the centre is to manage the international database of ADR reports received from national centers. The UMC has established standardized reporting by all National centers and facilitated communication between countries to promote rapid identification of signals. Another project at the UMC is the creation of an ADR monitoring system for herbal and traditional medicines.

The national centers in collaboration with the UMC have achieved a great deal in:
- Collecting and analyzing case reports of ADRs,
- Distinguishing signals from background “noise”,
- Making regulatory decisions based on strengthened signals, and
- Alerting prescribers, manufacturers, and the public to new risks of adverse structures.

Collecting spontaneous reports of suspected ADRs remains their core activity. Scope of activities of national centers has expanded to include communication of information about benefit, harm, and risk to practitioners, patients and the public. Certain centers have established active surveillance programs using record linkage.

## Role of the Hospitals and Academia

A number of institutions have developed adverse reaction and medication error surveillance systems in their centers. In the last decade or so, ADR monitoring was recognized as an essential quality assurance activity with most accreditation agencies such as national Accreditation Board for Hospitals, Joint Commission on Accreditation for Hospitals Organization, and Medical Council of India insisting upon its establishment.

## Role of the Industry

Recent advances in the technologies have helped the pharmaceutical industry to develop safer drugs. High regulatory standards set at national and international levels along with communication between the industry and the regulatory authorities have helped better information of the drugs available to the doctors, public, etc.

## Can Pharmacovigilance Prevent New Drug Tragedies from Developing?

Some of the examples of withdrawals from the market after it was approved for commercial use as a result of spontaneous reporting are listed in Table 1.[11]

Adverse drug reactions are the fourth to sixth leading cause of morbidity in United States of America.[12] More than 10% of hospital admissions are due to adverse drug reactions.[13] Some countries spend up to 15–20% of their hospital budget dealing with drug complications.[14]

Adverse cutaneous drug reactions are the most frequent of all manifestations of drug sensitivity, 24% of all adverse drug reactions in one study.[15]

Dermatologists have the greatest opportunity in reporting the various reactions that can happen as they come across majority of these drug reactions, prescribed by all sectors of health system such as public and private hospitals, general practitioners, nursing homes, retail dispensaries, and clinics for traditional practice.

**Table 1: Drugs withdrawn from the market after being approved for commercial use as a result of spontaneous reporting**

| Brand name | Reason for withdrawal | Year of manufacture | Year of withdrawal |
|---|---|---|---|
| Bromfenac | Serious hepatotoxic effect | 1997 | 1998 |
| Encainide | Excessive mortality | 1987 | 1991 |
| Flosequinan | Excessive mortality | 1992 | 1993 |
| Temafloxacin | Haemolytic anemia | 1992 | 1992 |
| Benoxaprofen | Liver necrosis | 1982 | 1982 |
| Mibefradil | Multiple drug interaction | 1997 | 1998 |
| Terfenadine | Fatal cardiac arrhythmia | 1985 | 1998 |

The success or failure of any spontaneous reporting system depends on the active participation of reporters.

Dermatologists can and should take an active role in observing, detecting, and reporting unwanted and unexpected drug reactions.

In clinics and hospitals where pharmacovigilance centers are not functioning, the dermatologists should be educated about the process of reporting to the national drug information centre online. Alternatively, the dermatology association at the national level and also at regional level can also have an adverse drug reaction reporting system online in their websites where the doctor can report the event.

## What Should be Reported?

- For "new" drugs – report all suspected reactions, including minor ones. (In many countries drugs are still considered "new" up to 5 years after marketing authorization.)
- For established or well-known drugs report all serious or unexpected (unusual) suspected ADRs
- Report if an increased frequency of a given reaction is observed
- Report all suspected ADRs associated with drug–drug, drug–food, or drug–food supplements (including herbal and complementary products) interactions
- Report ADRs in special fields of interest such as drug abuse and drug use in pregnancy and during lactation
- Report when suspected ADRs are associated with drug withdrawals
- Report ADRs occurring from overdose or medication error
- Report when there is lack of efficacy or when suspected pharmaceutical defects are observed

## How to Report ADRs?

Local case report forms (CRF) should be obtained from the National Drug Regulatory Authority. Some countries have included CRF in their national formularies.[11]

A CRF should have at least four sections that should be completed.

1. Patient information
   - Patient identifier
   - Age at time of event or date of birth
   - Gender and
   - Weight
2. Adverse event or product problem
   - Description of event or problem
   - Date of event
   - Date of report
   - Relevant tests/laboratory data (if available)
   - Other relevant patient information/history
   - Outcomes attributed to adverse event
3. Suspected medication(s):
   - Name (INN and brand name)
   - Dose, frequency, and route used
   - Therapy date
   - Diagnosis for use
   - Event abated after use stopped or dose reduced
   - Batch number
   - Expiration date
   - Event reappeared after reintroduction of the treatment and
   - Concomitant medical products and therapy dates
4. Reporter
   - Name, address and telephone number and
   - Speciality and occupation

## Useful Websites

- WHO www.who.int/medicines/
  Section: quality assurance and safety: medicines
- WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre) www.who-umc.org
- Web site of Central Drugs Standard Control Organization. Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India: http://cdsco.nic.in/

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