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PHARMACOVIGILANCE AS A PROTECTIVE SHIELD TO PREVENT ADVERSE EFFECTS OF PHARMACEUTICAL PRODUCTS

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ABSTRACT

Pharmacovigilance (PV, or PhV), also known as drug safety, is the pharmaceutical science relating to the "collection, detection, assessment, monitoring, and prevention" of adverse effects with pharmaceutical products. The etymological roots for the word "pharmacovigilance" are: pharmakon (Greek for drug) and vigilare (Latin for to keep watch). As such, pharmacovigilance heavily focuses on adverse drug reactions (ADR), which are defined as any response to a drug which is noxious and unintended, including lack of efficacy (the condition that this definition only applies with the doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological disorder function was excluded with the latest amendment of the applicable legislation). Medication errors such as overdose, and misuse and abuse of a drug as well as drug exposure during pregnancy and breastfeeding, are also of interest, even without an adverse event, because they may result in an adverse drug reaction. Information received from patients and healthcare providers via pharmacovigilance agreements, as well as other sources such as the medical literature, plays a critical role in providing the data necessary for pharmacovigilance to take place. In order to market or to test a pharmaceutical product in most countries, adverse event data received by the license holder (usually a pharmaceutical company) must be submitted to the local drug regulatory authority. Ultimately, pharmacovigilance is concerned with identifying the hazards associated with pharmaceutical products and with minimizing the risk of any harm that may come to patients. Companies must conduct a comprehensive drug safety and pharmacovigilance audit to assess their compliance with worldwide laws, regulations, and guidance.

KEYWORDS: ADR, Drug safety, IND, NCE, NDA, ANDA, FDA.

INTRODUCTION

Pharmacovigilance is the process and science of monitoring the safety of medicines and taking action to reduce the risks and increase the benefits of medicines.[1] It is a key public health function. Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem. All medicines and vaccines undergo rigorous testing for safety and efficacy through clinical trials before they are authorized for use.[2]

Figure-1: Pharmacovigilance flowchart.

Drug Discovery Steps
Step 1: Discovery and Development.
Step 2: Preclinical Research.
Step 3: Clinical Research.
Step 4: FDA Drug Review.
Step 5: FDA Post-Market Drug Safety Monitoring.

Pharmacovigilance Process
Pharmacovigilance Process (Stage 1): Detection. Collection of Individual Case Safety Reports (ICSRs)
Pharmacovigilance Process (Stage 2): Assessment
Pharmacovigilance Process (Stage 3): Understanding the drug safety profile
Pharmacovigilance Process (Stage 4): Prevention of adverse effects
The major components of a pharmacovigilance system are data collection, which can be **passive**, **active**, or **mandatory**, and **data analysis with reporting**.[3]

Phase: Phase refers to the four phases of clinical research and development: I – small safety trials early on in a drug's development; II – medium-sized trials for both safety and efficacy; III – large trials, which includes key (or so-called "pivotal") trials; IV – large, post-marketing trials, typically for safety reasons.[4]

Aims of pharmacovigilance: Maintain a robust monitoring system for new safety issues. Implement effective approaches to minimize risk. Install procedures for rapid decision making and triggering actions in case of (immediate) safety concerns.
The three main types of post-marketing Pharmacovigilance are.
Drug safety surveillance.
Drug abuse and adverse effects monitoring.
Safety monitoring of new products.[5]

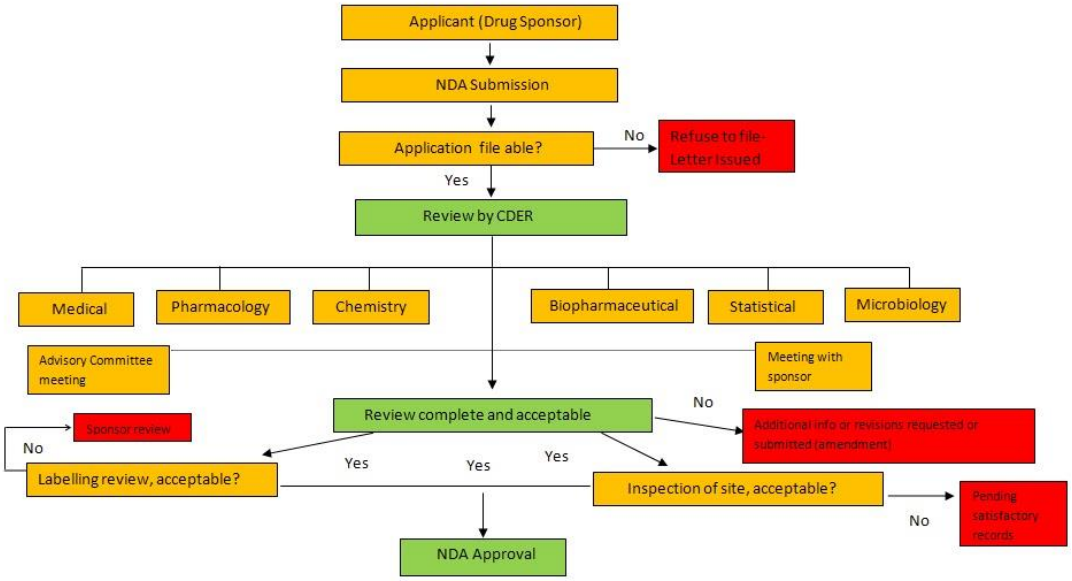

Figure-2: NDA processing.

Theme: Drug Safety / Pharmacovigilance. The primary motto of any drug safety system is premium non noncore (first, do no harm) in the field of heavily drug-reliant modern medicine. The phrase is Pharmacovigilance a Good Career option for professionals where they need to work closely with regulatory compliance, medical affairs, and clinical research to ensure effective identification, evaluation, and management of ADRs.[6]

The rule of three means that you need three times as many subjects to observe an event when you assume that the adverse event of interest does not normally occur in the absence of the medication.[7]

Data Entry: A seemingly repetitive and inconsequential step in the process but something that forms the basis of good reporting. The quality of data entry affects the further processing of the case. In pharmacovigilance, case processing is a fundamental activity. It provides data for the analysis of adverse effects that allows to detect new safety concerns and to periodically assess the benefit-to-risk ratio associated with the use of a pharmaceutical product.

ARISg is also one of the most used software in pharmacovigilance used by pharmaceutical companies. What is Argus in pharmacovigilance? ARISg is also one of the most used software in pharmacovigilance used by pharmaceutical companies.[8]

Oracle Argus is a comprehensive pharmacovigilance platform which enables pharmaceutical companies and clinical trial organizations to make faster and better safety decisions, optimize global compliance, and easily integrate risk management. day zero is the date on which an organization becomes aware of a publication containing the minimum information for an ICSR to qualify for submission. Awareness of a publication includes any personnel of that organization, or third parties with contractual arrangements with the

organization. Identification of the problem - The first step involves identifying whether an issue has occurred with a drug or a group of drugs. This can be done by monitoring adverse event reports, or through clinical studies and medical literature. Phase IV trials are also known as post-marketing surveillance trials. Phase IV trials involve the safety surveillance (pharmacovigilance) and ongoing technical support of a drug after it receives permission to be sold. Drug Safety and Pharmacovigilance" is not a single term.[9]

Figure-3: Drug Safety.

There is a slight difference between "Drug Safety" and "Pharmacovigilance." In short, we can say one is reactive, and the other is proactive. One is taking care of compliance and reporting, and the other is focused on interpreting signals. A type of clinical trial that studies the side effects caused over time by a new treatment after it has been approved and is on the market. These trials look for side effects that were not seen in earlier trials and may also study how well a new treatment works over a long period of time. The first step in testing a new treatment in humans.[10] Phase I clinical trial tests the safety, side effects, best dose, and timing of a new treatment. It may also test the best way to give a new treatment (for example, by mouth, infusion into a vein, or injection) and how the treatment affects the body. Phase II clinical trials tells doctors more about how safe the treatment is and how well it works.[11] Doctors also test whether a new treatment works for a specific cancer. They might measure the tumor, take blood samples, or check how well you can do certain activities. Phase III trials test if a new treatment is better than a standard treatment. It is the last phase of testing to be completed before the drug's details and clinical trial results are submitted to the regulatory authorities for approval of the drug's release on the open market. Phase IV trials find more information about long-term benefits and side effects. Phase V Clinical Trial means a post-registration clinical trial that is not required as a condition to, or for the maintenance of, any Marketing Approval or Pricing and/or Reimbursement Approval for a Licensed Product. Phase V Clinical Trials are commonly referred to as "post-marketing clinical trials".[12]

Figure-4: Pharmacovigilance as a protective shield from adverse effects.

Drug Safety is Pharmacovigilance. The primary motto of any drug safety system is premium non nocere (first, do no harm) in the field of heavily drug-reliant modern medicine. The FDA, as an active member of the WHO Programme for International Drug Monitoring, forwards all the reports anonymously to the global database. The FDA Pharmacovigilance Team carefully screens all the reports for new risk. Average starting Salary for

Pharmacovigilance Associate in India is around ₹2.0 Lakhs per year (₹16.7k per month). An undergraduate or postgraduate degree in Chemistry (subject) with an average of at least 50%. The study of pharmacy or pharmaceutical science at the graduate or postgraduate level. Medicine at the graduate or postgraduate level.[13]

Welcome to the Yellow Card reporting site. Report suspected side effects to medicines, vaccines, e-cigarettes, and medical device incidents, defective or falsified (fake) products to the Medicines and Healthcare products Regulatory Agency to ensure safe and effective use. An AE is considered serious when the patient outcome falls under any of the following seven categories: death, life threatening, hospitalization or hospital prolongation, disability, congenital anomaly, intervention required to prevent impairment, or an important medical event. An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.[14] There are several types of data entry services. These include basic, online, formatting, conversion, and transcription. Drug firms today must create comprehensive drug safety strategies amid an ever-changing regulatory environment. Pharmacovigilance key performance indicators (PV KPIs) are a set of quantifiable measures that a company uses to gauge its performance over time. These quantifiable measures can be used to indicate how a well a pharmacovigilance system is performing and whether the system is continually improving. Most health care professionals, especially nurses, know the **"five rights"** of medication use: the **right patient, the right drug, the right time, the right dose, and the right route**—all of which are generally regarded as a standard for safe medication practices.[15]

Figure-5: New Chemical Entity & New Drug Application.

IND: An investigational new drug may be approved by the FDA for use in one disease or condition but still be considered investigational in other diseases or conditions. Also called experimental drug, IND, investigational agent, and investigational drug.[16]

NCE: New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other application. It's important to note the difference between an NCE and a New Molecular Entity (NME). While an NCE has no active moiety, an NME contains an active moiety that has not yet been approved by the FDA or marketed in the U.S. The FDA (the US Food and Drug Administration) defines a new molecular entity (NME) as a new drug whose active ingredient is a chemical substance that is marketed for the first time in the United States. In other words, the FDA has not previously approved some of the moieties contained in a drug that has been endorsed. These NCE-1 dates indicate the first opportunity for generic drug companies to file Abbreviated New Drug Applications (ANDAs) for generic entry into branded drug markets. Generic launch is dependent on many factors, including FDA approval and patents.[17]

The 4 stages of drug development:
Step 1: Discovery and Development.
Step 2: Preclinical Research.
Step 3: Clinical Research.
Step 4: FDA Drug Review.
Step 5: FDA Post-Market Drug Safety Monitoring.

Types of medicines.

Liquid. The active part of the medicine is combined with a liquid to make it easier to take or better absorbed.
Tablet. The active ingredient is combined with another substance and pressed into a round or oval solid shape.
Capsules.
Topical medicines.
Suppositories.
Drops.
Inhalers.
Injections.
Chemical, approved and proprietary names are the three main types of name for pharmaceutical substances are

the chemical name, the approved (official or generic) name and the proprietary (brand, trade or invented) name.

NDA: The New Drug Application is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing.[18]

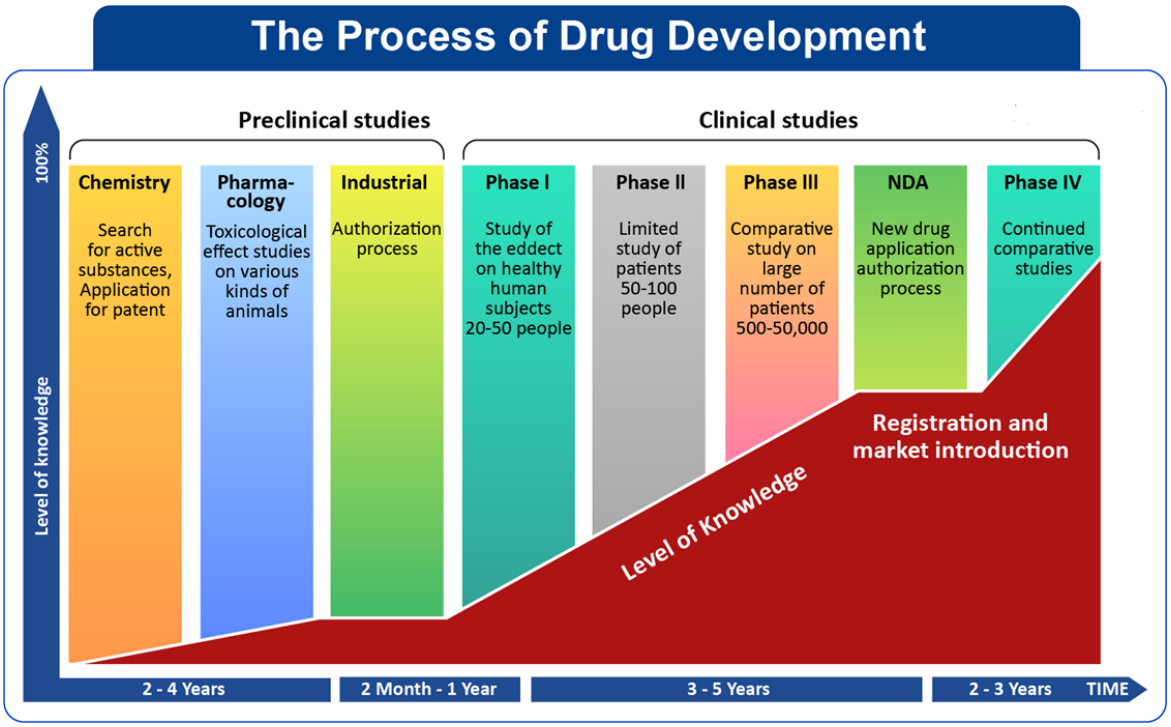

Figure-6: Drug development Process.

ANDA: An ANDA lists the new drug's established name, trade name (if any), chemical name, dosage form(s), and strength(s), route of administration, and proposed use. The ANDA asks for the name of the listed drug product to which the proposed generic is an equivalent. An Abbreviated New Drug Application (ANDA) contains data which is submitted to the FDA for the review and potential approval of a generic drug product whereas a New Drug Application (NDA) is the application through which sponsors formally propose the approval of a new pharmaceutical drug.[19,20]

CONCLUSION

Drug safety, sometimes also referred to as Safety Pharmacology or Pharmacovigilance, is a critical pre-clinical step in the drug development process. As new chemical entities (NCE) and biologic molecules are discovered, it is important to assure that these drugs do not cause any adverse "off-target" effects. All drugs have side effects, but the extent of their impact and severity varies from mild (such as mild itching or mild headache) to severe (such as severe rash, damage to vital organs, primarily the liver and kidneys, and possibly even death). Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem. All medicines and vaccines undergo rigorous testing for safety and efficacy through clinical trials [I-V] before they are authorized for use. Specific aims of pharmacovigilance are to: Maintain a robust monitoring system for new safety issues. Implement effective approaches to minimize risk. Install procedures for rapid decision making and triggering actions in case of (immediate) safety concerns. There is a slight difference between "Drug Safety" and "Pharmacovigilance." In short, we can say one is reactive, and the other is proactive. One is taking care of compliance and reporting, and the other is focused on interpreting signals. New Drug Application (NDA) & Abbreviated New Drug Application (ANDA) both are applicable with New Chemical Entity (NCE) for drug safety under pharmacovigilance.

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