



PHARMACOALERT NEWS LETTER



DRUG SAFETY ALERT, NEW DRUG MARKETED, DRUG INTERACTIONS AND BANNED DRUGS

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FROM THE DESK OF EDITORIAL TEAM

The Department of Pharmacology, Dr.RMLIMS, Lucknow, presents the third issue of its newsletter PHARMACOALERT. Continuing in our effort to bring forth the detailed information regarding Adverse Drug Reaction Reports, we are delving deep into the flow of data in PvPI after it has been submitted to the AMC and also an insight on how a 'Signal' is generated from the numerous reports we submit.

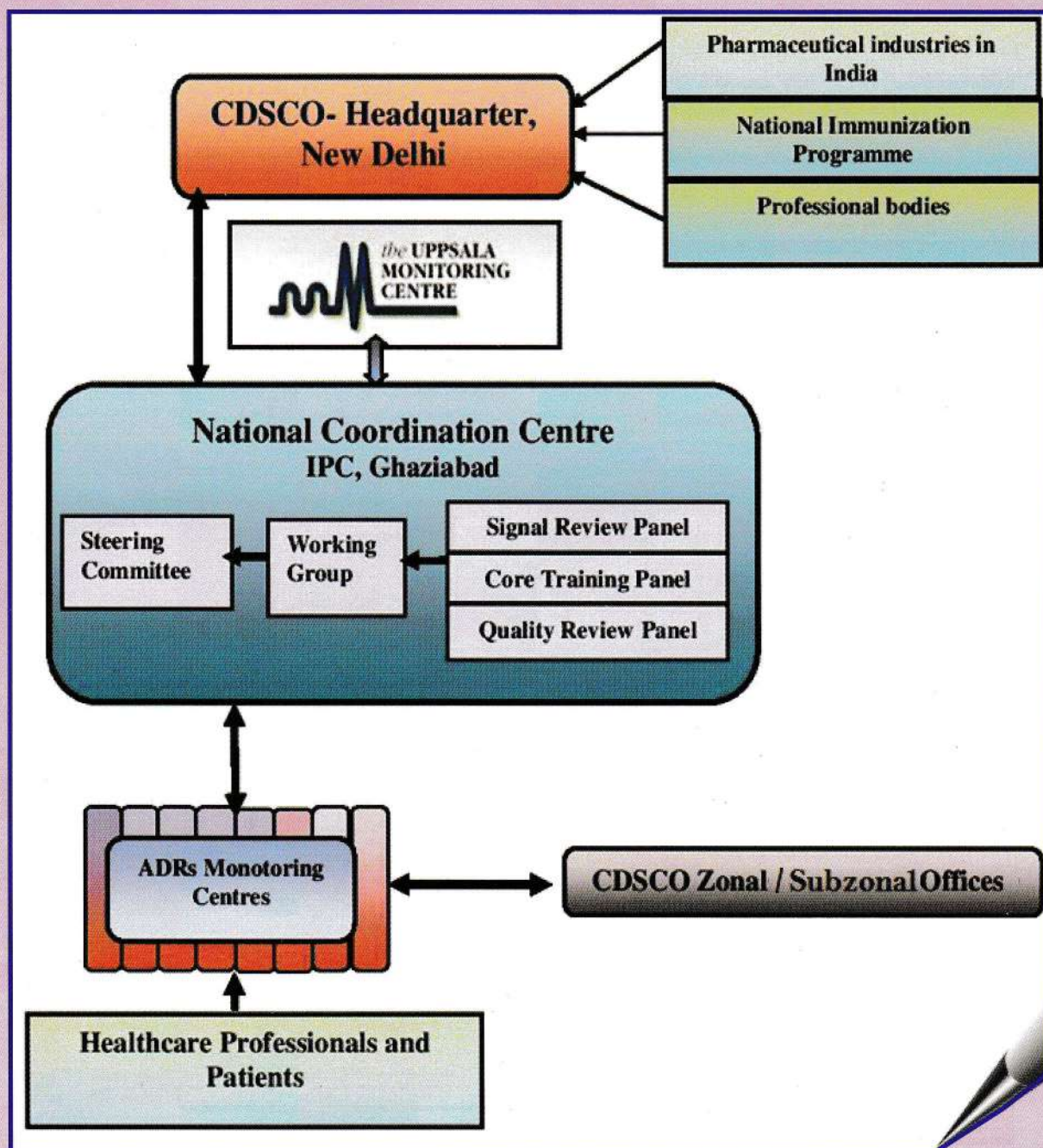
Apart from this, 'Prevention of Medication Errors' features in our regular column of "Medication Errors". Summary of the important drug approvals along with relevant important information about the drug recalls, alerts, nuggets from the past and latest news on coronavirus outbreak completes this issue of the newsletter.

Keep reading and enjoying.

Wishing you all a very Happy New Year 2020

DATA FLOW IN PHARMACOVIGILANCE

Once the Medical Institute is enrolled as an ADR Monitoring Centre (AMC) under PvPI, the AMC starts reporting Individual Case Safety Reports (ICSRs) to NCC via Vigiflow. These ICSRs are then assessed at NCC for quality of data and if found valid, they are further committed to the global drug monitoring centre “Uppsala Monitoring Centre” in Sweden. But if the data is not complete or valid, then the ICSRs are reverted back to their concerned AMC with the query or necessary comments, so that the respective ICSR can be corrected or completed and send to NCC again for evaluation. The data from NCC is also sent to CDSCO, as and when required. Following chart explains the flow of data at regional, national and international level.



Assessment of ICSRs:

The quality of the ICSR is assessed for completeness of information and is reviewed for:

- i. Quality of documentation: eg. completeness and integrity of data, quality of diagnosis, follow-up
- ii. Coding: Drugs name should be registered in a systematic way, for example by using the WHO Drug Dictionary (which is based on the ATC classification). For the coding of the adverse events the WHO Adverse Reaction Terminology (WHOART) and Internationally recognized terminology (eg. MedDRA) should be used.
- iii. Relevance with regards to the detection of new reactions, drug regulation, or scientific or educational value. The following questions especially may be asked:
 - New Drug- A new drug shall continued to be considered as new drug for a period of four years from the date of its first approval or its inclusion in Indian Pharmacopoeia (IP), whichever is earlier.
 - Unknown reaction- Not included in the Approved Summary of Product Characteristics.
 - Serious reaction- Results into either death, life threatening condition, hospitalization, or prolonged hospitalization, disability, congenital anomaly, required intervention to prevent permanent impairment/damage or any other medically important condition.
- iv. Identification of duplicate reports: Certain characteristics of a case (sex, age or date of birth, dates of drug exposure, etc.) maybe used to identify duplicate reporting.
- v. Causality assessment: The likelihood of a causal relationship between drug exposure and adverse events must be validated.

Utilization of the data:

The WHO has defined a signal as “Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously” An additional note says: “Usually more than one report is required to generate a signal, depending on the seriousness of the event and the quality of the information”.

Data collected in Pharmacovigilance can be used in a variety of ways:

- i. Signal generation and strengthening: A major aim of Pharmacovigilance is the early detection of signals with regard to possible adverse reactions. A signal may be strengthen by further analysis which can help the regulatory system in performing regulatory activities.
- ii. Drug regulation: After approval of a medicinal product, all available domestic and international safety information is continuously monitored by the drug regulatory authority and Marketing authorisation holder (MAH). The PvPI data can be useful in resolving the problems by adaptation of the approved product information (inclusion of new adverse effects and warnings).
- iii. Education: The information from PvPI data is useful in updating the knowledge of healthcare professionals during continuous medical education program on Pharmacovigilance.

DRUG SAFETY ALERT

(October - December 2019):

Sl. no.	Suspected Drugs	Adverse Drug Reactions
1	Levamisole	Stevens Johnson Syndrome
2.	Cephalosporin	Acute Generalized Exanthematous Pustulosis
3.	Cetirizine	Hiccups
4.	Cilostazole	Tinnitus
5.	Clozapine	Neural Tube Defects

USE OF PARACETAMOL TO TENDERIZE MEAT IN AFRICAN COUNTRIES:

Certain eateries in the West African nations like Nigeria and Ghana are using paracetamol to soften or tenderize meat, a cost cutting measure which is costing the health and lives of diners. For many eateries and even households the use of paracetamol cut down their cooking time, thereby saving cash in terms of gas, kerosene or firewood as paracetamol softens a pot-full of meat within minutes. However, when paracetamol is used for cooking, it gets hydrolysed to 4-aminophenol which is highly acidic product and very toxic to the kidney. This has led to rise in the instances of renal failures and chronic kidney disease. The Nigeria Medical Journal noted that Chronic kidney disease (CKD) had become so prevalent in the country that it has "become a public health problem in Nigeria." The Nigerian FDA has warned against this practise and has called for a ban on the use of paracetamol for cooking meat.

DRUG APPROVAL

Levonadifloxacin: DCGI has recently approved Levonadifloxacin tablet and injectable form for adults (≥ 18 years of age) for the treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) including diabetic foot infections and concurrent bacteraemia caused by susceptible isolates of Gram-positive organisms like *Staphylococcus aureus* (methicillin-resistant, methicillin-susceptible, quinolone-resistant, quinolone-susceptible isolates), *Streptococcus pyogenes*, *Enterococcus faecalis*, *Streptococcus dysgalactiae* ssp. *dysgalactiae*, *Streptococcus agalactiae*. It is a novel broad-spectrum anti-MRSA agents belonging to the benzoquinolizine subclass of Quinolone. Various in vitro and in vivo studies have established their antimicrobial spectrum against clinically significant Gram-positive, Gram-negative, atypical, and anaerobic pathogens.

List of Important Drugs approved in December 2019 (Available from FDA)

Sl	Name of the Drug	Mechanism of Action	Indications	Date of Approval
1	Golodirsen	Gene Therapy-Include Exon 53 Skipping in The Dystrophin Gene	Duchenne muscular dystrophy	12/12/2019
2	Enfortumab vedotin-ejfv	Nectin-4-directed antibody-drug conjugate	Refractory bladder cancer	18/12/2019
3	Lumateperone tosylate	Antagonist of 5HT _{2A} , Modulate D1, D2, Modulate NMDA and AMPA activity Via mTOR pathway	Schizophrenia	20/12/2019
4	Lemborexant	Orexin receptor antagonist	Insomnia	20/12/2019
5	Fam-trastuzumab deruxtecan-nxki	HER2-directed antibody and topoisomerase inhibitor conjugate	HER2-positive Metastatic breast cancer	20/12/2019
6	Ubrogepant	Calcitonin gene-related peptide receptor antagonists	Acute treatment of migraine with or without aura in adults	23/12/2019

PREVENTION OF MEDICATION ERROR

Medication errors can occur in any steps during the process of medication use. It is foremost important to identify and analyse individual problems, and deficiencies and the fault in systems that lead to medication errors. It requires a multidisciplinary approach of Clinical pharmacologists, physicians, clinical pharmacists, etc. and information technology to tackle the menace of medication errors. There should also be a focus on the special population, such as children and the elderly. There are various tools which can be applied during during the process of medication use to prevent medication errors.

Prevention of errors during prescribing medications:

As most of the errors occur during this stage care should be taken to minimize the errors in prescribing. All prescription orders should be legible, to reduce handwriting errors, complete, and reviewed at the nursing station and by the pharmacist to ensure the intended interpretation and transcription. Medication name, dosage form, dose (in metric system except for therapies that use standard units such as insulin), route, and frequency should be properly mentioned. It should have a brief description of the indication of the prescribed medication. Use of abbreviations should be avoided. The prescriber should avoid vague instructions such as “take as directed” as the sole direction for use. Physicians should use a leading zero to the left of a dose <1 and avoid the use of a terminal zero to the right of the decimal point to minimize ten-fold errors in drug strength and dosage. Mentioning the age of the patient and weight when appropriate in the prescription order can help the dispensing health care professionals to double check the appropriateness of the drug and dosage. Clinical pharmacist-assisted rounds should be encouraged For they can consistently review prescriptions written by clinicians, as they are familiar with the institution's formulary, can assist physicians in selecting medications from among those drugs that are stocked for the patient during the hospital stay as well as when he gets discharged by addressing the discrepancies of medications in the discharge papers, addressing polypharmacy and focusing on the rational use of drugs to minimize the threat to patient health. The speed and accuracy of transcription are improved with electronic order transcription like computerized physician order entry (CPOE). It is inbuilt with decision support that may be useful to target the potentially inappropriate prescriptions errors or wrong medications and alert the health-care professionals on clinically relevant warnings. It also helps in eliminating errors related to illegible handwriting. CPOE will particularly improve communication efforts during the transfer of care of the patients.

Prevention of errors during dispensing medications :

Prescription orders should be reviewed by a pharmacist before dispensing and any concern related to prescription order should be clarified. The pharmacists should counsel patients at the time of dispensing to verify the accuracy of dispensing and the patient's understanding of proper medication use. Whenever possible an independent check by another staff should be done to assess the accuracy of dispensing. Automated dispensing device, use of bar code technology help in reducing the human factors errors, such as “look-alike” and sound-alike” drugs and to identify the right patient, the right drug, and the right dosage. The dispensing area should be designed with proper lighting, ventilation to provide a good working environment so as to minimize errors. There should be sufficient staff and other resources to match the workload. Product inventory should be arranged to help differentiate medications from one another. High alert/high-risk medications need to be stored under lock and key with label of high-risk medications and inventory shall be maintained. Pharmacy staff should triple check replenishment of regular medication stock and automated dispensing cabinets to ensure accuracy of the medications and their placement. An initial and ongoing trainings of the pharmacy staff on standard of accurate dispensing process are needed.

Prevention of errors during administering medications:

The administration phase of medication delivery is a significant step to intervene to eliminate the sources of medical error. In all health care establishments, the person or staff administering medication should be aware about the indication, precautions, warnings expected outcomes, potential adverse reactions, interactions of the drug with concomitantly administered drug or food, actions to take when adverse reactions or interactions occur. Medication administration records (MARs) should be maintained properly with proper recording of the time, date, and route of ordered drug. Incorporating the MAR into a computerized system results in typed orders and administration information which decreases the potential for errors. It is always advisable to track the patient's current medications and those prescribed during discharge.

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2. Nandave M, Kaur S, Medhi B. A. Medication Errors. In: Medhi B, Prakash A editors. *Advanced Pharmacology*. Hyderabad: PharmaMed Press; 2015. p.12-34

**FROM THE PAST
IMPORTANT EVENTS IN JANUARY:**

January 1, 1660 : Samuel Pepys began his famous diary in which he chronicled life in London including the Great Plague of 1664-65

January 1896 German physicist Wilhelm Röntgen announces his discovery of X-rays stumbled in November, published in December and announced in January later, since his notes were burned and information percolated to different places at definite times exact date still remains unearthed

January 7, 1714 : A patent was issued for the first typewriter designed by British inventor Henry Mill "for the impressing or transcribing of letters singly or progressively one after another, as in writing, became the foundation for granting Intellectual Property Rights.

January 21, 1677: 1st medical publication in America (pamphlet on smallpox), published in Boston.

January 27, 2017: For the first time in the world, scientists created metallic hydrogen by applying almost five million atmospheres of pressure to liquid hydrogen. It is the first time a state of hydrogen has existed in a metallic state on Earth. In its metallic state, hydrogen could act as a genuine superconductor and could revolutionize everything from energy storage to rocketry.

**CORONAVIRUS OUTBREAK :
A PUBLIC HEALTH CONCERN**

An infection with a novel coronavirus (2019-nCoV) has been reported from China. As 25th January 2020, a total of 1287 cases and 41 deaths were reported in 29 provinces of China. In addition, 28 cases have been confirmed outside Chinese mainland. There is no specific drug as such. The researchers are claiming that anti-retroviral drugs, like some **protease inhibitors** can be repurposed for the treatment of this 2019-nCoV infection. Management of this infection include general supportive measures under full infection control protocols, and will conform to management of respiratory involvement according to severity, other bacterial co infection, etc. On. 30th January 2020, India's first case of coronavirus has been reported from Thrissur, Kerela in a medical student who has been exposed to the virus while studying medicine in Wuhan district of China.