



PHARMACOALERT

NEWS LETTER



Drug Safety Alert, New Drug Marketed, Drug Interactions and Banned Drugs

Editorial Committee:

Patron:

Dr. A K Tripathi,
Director, Dr. RMLIMS

Chief Editor: Dr. Atul Jain

Editor: Dr. Arpita Singh

Co-editors:

Dr. Pooja Shukla
Dr. Joonmoni Lahon

Members:

Dr. Chandresh Kr. Gupta
Dr. Laxman Verma
Dr. Divya R
Dr. Kritika Prashad
Mr. Saket Verma

CONTENTS

- Consumer ADR Reporting form
- Drug Safety Alerts (January February 2020)
- Causes of Medication Error
- Artificial Intelligence in Drug Discovery
- Drugs approved (January-February 2020)
- Palforzia –Drug for Peanut Allergy
- From the past

PUBLISHED MONTHLY BY THE
DEPARTMENT OF PHARMACOLOGY,
DR. RAM MANOHAR LOHIA
INSTITUTE OF MEDICAL SCIENCES,
LUCKNOW



FROM THE DESK OF EDITORIAL TEAM

Department of Pharmacology, Dr.RMLIMS, Lucknow, is pleased to present the February issue of its newsletter.

In order to ensure patient safety, PvPI has issued forms in different vernacular languages, thus we are here sharing with you the consumer ADR reporting form in Hindi with a request to kindly propagate it among the Consumers and general public so that they can directly report ADRs as first hand information and also become part of our national programme.

Continuing in our effort to bring forth new developments in the field of medicine, in this issue we have tried to give insight into use of 'Artificial Intelligence' in the world of drug discovery.

In the newer drugs approved an interesting discovery is the new drug that has been approved for the patients of peanut allergy by FDA for the age group of 4 years to 17 years. Though the manufactures do not claim to do wonders but its still a ray of hope in the management of children suffering from peanut allergy who accidentally ingest the allergen.

Information pertaining to drug safety alert, new drugs, etc. and our regular column on Medication Error is there as before. In Historical titbits from the past this time we share with you the anecdote related to one of the most important discovery of the science i.e Double Helix Structure of the DNA. Another interesting thing is that on the same date years before our very own Sir C V Raman discovered Raman Effect for which he was awarded Nobel Prize too. **To commemorate this great feat we celebrate our National Science Day on 28th of February 2020 every year**

Keep reading and enjoying.



MEDICINES SIDE EFFECT REPORTING FORM (FOR CONSUMERS)

औषधि दुष्प्रभाव सूचना फॉर्म (उपभोक्ताओं के लिए)

Indian Pharmacopoeia Commission, National Coordination Centre - Pharmacovigilance Programme of India, Ministry of Health & Family Welfare, Government of India.

भारतीय भेषज संहिता आयोग, राष्ट्रीय समन्वय केंद्र – भारतीय फार्माकोविजिलेंस कार्यक्रम,
स्वास्थ्य एवं परिवार कल्याण मंत्रालय, भारत सरकार।

1. Patient Details/ रोगी का विवरण				
Patient Initials/ रोगी के आद्याक्षर:		Gender/ लिंग (v): Male/ पुरुष ☐ Female/ स्त्री ☐		Age (Year or Month)/ आयु (वर्ष या माह):
2. Health Information/ स्वास्थ्य संबंधी जानकारी				
a. Reason(s) for taking medicine(s) (Disease/Symptoms)/ दवा(दवाएं) लेने का कारण (रोग/लक्षण):				
b. Medicines Advised by/ दवाई की सलाह देने वाला (v): Doctor/ डॉक्टर ☐ Pharmacist/ फॉर्मासिस्ट ☐ Friends/Relatives/ मित्र/ रिश्तेदार ☐ Self (Past disease experienced/No past disease experienced)/ स्वयं (पूर्व बीमारी का अनुभव/पूर्व बीमारी का कोई अनुभव नहीं) ☐				
3. Details of Person Reporting the Side Effect/ दुष्प्रभाव की सूचना देने वाले व्यक्ति का विवरण				
Name (Optional)/ नाम (वैकल्पिक):				
Address/ पता:				
Telephone No/ टेलीफोन नं:		Email/ ईमेल:		
4. Details of Medicine Taking/Taken/ ली जा रही है / ली जा चुकी दवाई का विवरण				
Name of Medicines/ दवाइयों के नाम	Quantity of Medicines taken (e.g. 250 mg, Two times a day)/ ली गई दवाई की मात्रा (उदाहरण के लिए 250 मिग्रा, एक दिन में दो बार)	Expiry Date of Medicines/ दवा के निष्क्रिय होने की तिथि	Date of Start of Medicines/ दवाइयां आरंभ करने की तिथि	Date of Stop of Medicines/ दवाइयां रोकने की तिथि
Dosage form/खुराक का स्वरूप (v) : Tablet/ गोली (टेबलेट) ☐ Capsule/ कैप्सूल ☐ Injection/ इंजेक्शन ☐ Oral Liquids/ मौखिक तरल ☐ If Others (Please Specify.....)/यदि अन्य (कृपया निर्दिष्ट करें.....)				
5. About the Side Effect/ दुष्प्रभाव के बारे में				
When did the side effect start?/ दुष्प्रभाव की शुरुआत कब हुई थी?		Side Effect is still Continuing (Yes/No)/		
When did the side effect stop?/ दुष्प्रभाव कब समाप्त हुआ था?		क्या दुष्प्रभाव जारी हैं (हां/ नहीं):		
6. How bad was the Side Effect? (Please v the boxes that Apply)/ दुष्प्रभाव कितने हानिकारक थे? (कृपया जो लागू हो, उस पर v का निशान लगाएं)				
☐ Did not affect daily activities/ दैनिक गतिविधियां प्रभावित नहीं हुई थी		☐ Affect daily activities/ दैनिक गतिविधियां प्रभावित हुई		
☐ Admitted to hospital/ अस्पताल ले जाना पड़ा		☐ Death/ मृत्यु		
☐ Others/ अन्य				
7. Describe the Side Effect (What did you do to manage the side effect?)/ दुष्प्रभाव की व्याख्या करें (आपने दुष्प्रभावों से छुटकारा प्राप्त करने के लिए क्या किया)?				

This reporting is voluntary, has no legal implication and aims to improve patient safety. Your active participation is valuable. The information provided in this form will be forwarded to ADR Monitoring Centre for follow-up. You are requested to cooperate with the programme officials when they contact you for more details. Please do report even if you do not have all the information.

यह रिपोर्टिंग स्वैच्छिक है, कोई कानूनी निहितार्थ नहीं है और इसका लक्ष्य मरीज की सुरक्षा में सुधार करना है। आपकी सक्रिय भागीदारी मूल्यवान है। इस फॉर्म में दी गई जानकारी की अनुवर्ती कार्रवाई हेतु एडीआर निगरानी केंद्र को भेजा जाएगा। आपसे अनुरोध है कि आप कार्यक्रम के अधिकारियों का सहयोग करें जब वे अधिक जानकारी प्राप्त करने के लिए आपसे संपर्क करें। कृपया पूर्ण जानकारी न होने पर भी सूचित करें।

Please turn the page to read the instructions
निर्देशों को पढ़ने के लिए कृपया पेज पलटें

DRUG SAFETY ALERTS (JANUARY-FEBRUARY 2020)

Sl. No.	Suspected Drugs	Indication	Adverse Drug Reactions/ Safety Concern
1	Lorcaserin ¹	Weight Management	Increased risk of cancer
2.	Clozapine ¹	Schizophrenia	Constipation, progressing to serious bowel complications
3.	Disulfiram ²	Antidotes, Detoxifying Agents & Drugs Used in Substance Dependence	Skin Hyperpigmentation
4.	Fluconazole ²	Treatment of systemic candidiasis, mucosal candidiasis, pityriasis versicolor, prevention of fungal infections in patients with malignancy.	Mouth Ulceration
5.	Olanzapine ²	Schizophrenia	Hyponatremia
6.	Piperacillin+Tazobactam ²	Treatment of LRTI/UTI/Intra abdominal infections, skin and skin structure infections, bacterial septicemic polymicrobial infections	Blurred Vision

1. <https://www.fda.gov/drugs/drug-safety-and-availability/2020-drug-safety-communications>

2. <http://www.pvpi.in/das.html> (preliminary analysis of Adverse Drugs Reactions from the PvPI database)

CAUSES OF MEDICATION ERRORS

There have been numerous efforts to reduce medications error, the first step in providing a solution is identifying the root cause of errors. Thus, WHO has taken an initiative by reviewing different literature and the available data to tabulate different factors associated with the Medication Errors.

Factors associated with health care professionals

- Lack of therapeutic training
- Inadequate drug knowledge and experience
- Inadequate knowledge of the patient
- Inadequate perception of risk
- Overworked or fatigued health care professionals
- Physical and emotional health issues
- Poor communication between health care professional and with patients

Factors associated with patients

- Patient characteristics (e.g., personality, literacy and language barriers)
- Complexity of clinical case, including multiple health conditions, poly pharmacy and high-risk medications environment (e.g., lighting, temperature and ventilation)

Factors associated with medicines

- Naming of medicines (e.g. *Look Alike, Sound Alike Drugs*)
- Labelling and packaging

Primary-secondary care interface

- Limited quality of communication with secondary care
- Little justification of secondary care recommendations

Factors associated with the work environment

- Workload and time pressures
- Distractions and interruptions (by both primary care staff and patients)
- Lack of standardized protocols and procedures
- Insufficient resources
- Issues with the physical work environment

Factors associated with tasks

- Repetitive systems for ordering, processing and authorization
- Patient monitoring (dependent on practice, patient, other health care settings, prescriber)

Factors associated with computerized information systems

- Difficult processes for generating first prescriptions (e.g. drug pick lists, default dose regimens and missed alerts)
- Difficult processes for generating correct repeat prescriptions
- Lack of accuracy of patient records
- Inadequate design that allows for human error

Examples of Look Alike Sound Alike Drugs



Ref: Adopted from: Medication Errors Technical Series on Safer Primary Care by WHO

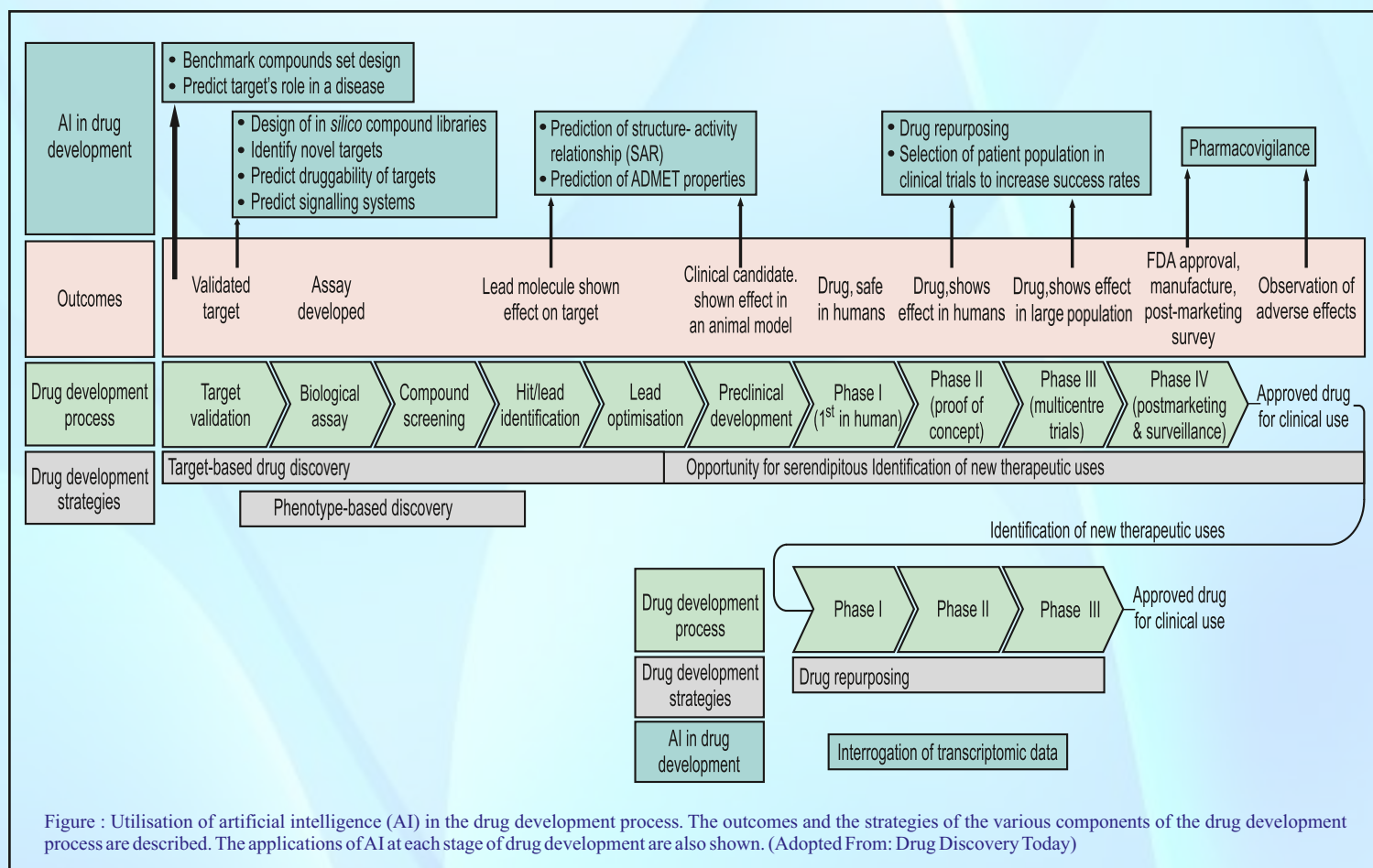
ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY

Artificial Intelligence (AI) is described as the use of techniques that enable computers to mimic human behaviour. This process includes acquiring information, developing rules for using the information, drawing approximate or definite conclusions and self-correction.

The task of finding successful new drugs is daunting and predominantly the most difficult part of drug development. This is caused by the vast size of what is known as chemical space, which is estimated to be in the order of 10^{60} molecules. Developing a new drug costs an average of nearly \$2.6 billion and may take more than a decade. AI will play a crucial role in curtailing this sum and time frame.

The technologies that incorporate AI have become versatile tools that can be applied ubiquitously in various stages of drug development, such as identification and validation of drug targets, designing of new drugs, drug repurposing, improving the R&D efficiency, aggregating and analysing biomedicine information and refining the decision making process to recruit patients for clinical trials. These potential uses of AI provide the opportunity to counter the inefficiencies and uncertainties that arise in the classical drug development methods while minimising bias and human intervention in the process.

AI implementation in clinical trial decision making can help the researchers to gather, analyse and gain insights from clinical trial data quickly. As one of the most heavy tasks in drug development and clinical trials is to create large datasets that capture a vast number of variables of patient data. AI can help generate significant results from this complex data.



Challenges of using AI in Drug Research

For an individual to be efficient in drug development using AI, the individual should know how to train algorithms, requiring domain expertise. It requires AI experts and medicinal chemists can work closely together, because the former will be able to help in analysing huge datasets and the latter can train machines, set algorithms or optimise the analysed data for a speedier and accurate drug development process.

Despite the benefit of AI in speeding up drug development, role of real experiments cannot be questioned as clinical trials provide real time human data and thus despite huge use of technology the data from trials is still desired.

First drug under development entirely by ARTIFICIAL INTELLIGENCE

A drug candidate DSP- 1181 is the first drug being developed entirely by AI. The drug which is a long-acting and potent serotonin 5-HT_{1A} receptor agonist will enter Phase I trials in Japan for obsessive-compulsive disorder. This drug has been developed discovered and readied in a short span of less than 12 months which has been possible with the help of AI.

Ref: <https://www.outsourcing-pharma.com/Article/2020/01/30/AI-developed-drug-goes-to-trial>
Kit-Kay Mak, Mallikarjuna Rao Pichika. Artificial intelligence in drug development: present status and future prospects. Drug Discovery Today, 2019; 24(3): 773-780.
Hongming Chen, Ola Engkvist, Yinhai Wan, et al. The rise of deep learning in drug discovery. Drug Discovery Today, 2018; 23(6): 1241-1250.

PALFORZIA

The drug that doesn't "cure" peanut allergy but can reduce the severity of its reaction

- Peanut allergy is a condition in which the body's immune system mistakenly identifies even small amounts of peanut as harmful.
- Symptoms can develop within seconds of exposure and may include skin reactions (e.g., hives, redness or swelling), digestive discomfort.
- Severe symptoms can be seen as constriction of the throat and airways, and loss of adequate blood flow to vital organs of the body.
- The U.S Food and Drug Administration (FDA) announced the approval of the peanut allergy drug Palforzia on January 31, 2020.
- "Peanut allergy affects approximately 1 million children in the U.S. and only 1 out of 5 of these children will outgrow their allergy. As there is no cure, allergic individuals must strictly avoid exposure to prevent severe and potentially life-threatening reactions"
- In India with a population of over a billion, some estimates suggest up to 3 per cent of Indians may already have food allergies, the majority of these are under 40 years of age."
- "Food allergies have been known to roughly cause 30,000 emergency treatments and 100 to 200 deaths per year.
- **Up to 3 million Indians may have peanut allergy alone (validation of this data is still needed due to lack of specific studies).**

PALFORZIA (Peanut (Arachis hypogaea) Allergen Powder-dnfp) is an oral immunotherapy for gradual desensitization and maintenance to protect peanut-allergic individuals in case of accidental exposure.

- This is the first FDA-approved treatment ever for food allergies.
- Though the mechanism of action has not been established, it has been found to reduce the allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut.
- Treatment with Palforzia consists of three phases: Initial Dose Escalation, Up-Dosing, and Maintenance.
- Treatment with Palforzia may be initiated in individual's age 4 through 17 years with a confirmed diagnosis of peanut allergy and may be continued in individuals 4 years of age and older.
- Powder for oral administration supplied in 0.5 mg 1 mg, 10 mg, 20 mg and 100 mg Capsules or 300 mg Sachets
- Oral administration should be given by opening capsule(s) or sachet and empty the entire dose of PALFORZIA powder onto refrigerated or room temperature semisolid food and consumed orally

ADVERSE EFFECTS

- Abdominal pain, itching, tingling in the mouth, nausea, vomiting, cough, runny nose, throat irritation, tightness, hives, wheezing, shortness of breath and anaphylaxis

CONTRAINDICATION

- Uncontrolled asthma
- History of eosinophilic esophagitis or other eosinophilic gastrointestinal disease

WARNING

- Do not swallow
- Do not inhale capsule or powder

PALFORZIA REMS PROGRAM

- PALFORZIA is available only through a restricted program under a **Risk Evaluation and Mitigation Strategy (REMS)** called the **PALFORZIA REMS** because of the risk of anaphylaxis

<https://www.downtoearth.org.in/news/food-allergies-on-the-rise-43889>
<https://www.fda.gov/media/134838>



DRUGS APPROVED IN JANUARY –FEBRUARY 2020

SI No.	Name of the Drug	Mechanism of Action	Indications	Date of Approval
1	Avapritinib	Tyrosine kinase inhibitor that targets PDGFRA and PDGFRA D842 mutants	To treat adults with unresectable or metastatic gastrointestinal stromal tumor (GIST)	9/01/20
2	Teprotumumab-trbw	Not been fully characterized binds to IGF-1R and blocks its activation and signalling [*]	To treat Thyroid eye disease	21/01/20
3	Tazemetostat	Selective EZH2 inhibitor [^]	To treat epithelioid sarcoma	23/01/20
4	Lactitol	Osmotic laxative	Chronic idiopathic constipation (CIC) in adults	12/02/20

<https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2020>

^{*} https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761143s000lbl.pdf

[^] https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212608s000lbl.pdf

FROM THE PAST-IMPORTANT EVENTS IN FEBRUARY

February 28: National Science Day is celebrated in India on this date each year to mark the discovery of the Raman effect by Indian physicist Sir C. V. Raman on 28 February 1928.

February 28: The Day Scientists Discovered the Double Helix

Nowadays, the structure of DNA is well-known for life science research, and even the general public are familiar with it. Nevertheless, have you thought of who discovered the secret of life in the first place? *On February 28, 1953, American molecular biologist James D. Watson and British biologist Francis H.C. Crick announced that they have determined the double-helix structure of DNA.*

Medical historian Dr. Howard Markel revisits moments that changed the course of modern medicine.

The place: The Eagle, a genial pub and favourite luncheon spot for the staff, students and researchers working at the University of Cambridge's old Cavendish laboratory on nearby Free School Lane.

The date: Feb. 28, 1953, a day when real, honest-to-goodness history was made.

The time: 12 noon.

Two men entered the noisy pub to create even more noise. The first was a tall, gangly, 25-year-old American bacteriologist with uncombed hair named James Watson. The second, Francis Crick, was a 37-year-old British physicist who, according to one of his scientific rivals, looked like "a bookmaker's rout."

With booming voices and youthful bravado, the odd duo bragged that they, in the words of Francis Crick -- or at least in the memory of James Watson recalling the words of Francis Crick -- "We have discovered the secret of life." Indeed, they had that very morning, the two men worked out the double helix structure of deoxyribonucleic acid, better known to every first-grader as DNA.

Mind you, they did not discover DNA. That scientific feat was actually accomplished in 1869 by Friedrich Miescher, a physiological chemist working in

Basel, Switzerland. Miescher determined that DNA, a nucleic acid found in the cell's nucleus, was comprised of sugar, phosphoric acid, and several nitrogen containing bases. But for decades, no one quite knew much about its precise function.



February will also be remembered in future if this experiment to display data on your skin fully succeeds:

In February 2018, a research team from the University of Tokyo unveiled semiconductor technology that can read the body's vital signs, and display them on a thin plastic material laid over your skin.

The display is made up of 16 by 24 micro LEDs and can be used to read your heart rate. The information can also be viewed on your smart device or sent directly to a medical professional.

Few very famous people who contributed to science in great manner were also born in February

3 February 1821- The first female physician in the U.S., Elizabeth Blackwell (1821-1910)

12 February 1809- Author and naturalist Charles Darwin (1809-1882)

15 February 1564 - Astronomer and physicist Galileo Galilei (1564-1642)

<https://www.newscientist.com/article/2161447-electronic-skin-animates-heartbeat-on-the-back-of-your-hand/>

<https://interestingengineering.com/new-electronic-skin-puts-your-heartbeat-on-your-hand>

<https://www.scientificamerican.com/article/february-28-the-day-scientists-discovered-double-helix/>

<https://www.historyplace.com/specials/calendar/february.htm>