Eleventh Issue
July – Dec
2022

PHARMACOALERT

NEWSLETTER

Contents:

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DEPARTMENT OF PHARMACOLOGY
DR. RAM MANOHAR LOHIA INSTITUTE OF MEDICAL SCIENCES
LUCKNOW

From The Desk of Editorial Team

Greetings!!!

The Department of Pharmacology, Dr. RMLIMS, Lucknow, is pleased to present the current special issue of our newsletter 'PHARMCOALERT'. In this issue we have compiled various recent articles of interest like New Drug approved Spesolimab, Revised National List of Essential Medicines, iNCOVACC,the new Nasal vaccine for COVID 19 etc.

Our article on 'Pharmacovigilance Program of India' (PvPI) holds the key to safe and rational use of drugs. The relevant information about the working system of PvPI has been reiterated here. From this issue onwards, graphical representation of the number of ADRs reported by different departments of Dr.RMLIMS shall now be featuring in our newsletter. We congratulate and thanks the Department of Radiodiagnosis for reporting maximum number of ADRs during July-December.

In the newer drugs approved section, information about new drugs approved by US-FDA between July-December has been mentioned. "Spesolimab" approved by FDA in September 2022 for 'Generalized Pustular Psoriasis' is the new drug discussed in detail in this issue.

Further to update, The 'National List of Essential Medicines' (NLEM), 2022 was revised and released after a seven year gap by Ministry of Health and Family Welfare, Govt of India on 13 September 2022. The new list has added 34 medicines that were not in the NLEM-2015 and deleted 26 drugs from the previous list, bringing the total number of drugs in the NLEM-2022 to 384. Excerpts from the Report of Standing National Committee on drugs for revision of NLEM has been shared to light upon reasons for changes in the NLEM-2015.

The new hope in our fight against the pandemic of COVID-19 and world's first intranasal vaccine for COVID-19 iNCOVACC also find a place in this issue.

We are glad to share the glimpses of the national CME, on "Current Perspectives on Pharmacovigilance: Present Scenario & Future Challenges" organised by department of Pharmacology,under the aegis of Pharmacovigilance Programme of India (PvPI), Indian Pharmacopoeia Commission, MoHFW, Govt. of India on 6th August 2022 at Dr.RMLIMS. We are pleased to inform that, our 1st batch of postgraduates participated and won the third prize in National level poster competition on topic "Active Pharmacovigilance of SGLT2 Inhibitors" organised by Indian Pharmacovigilance Commission, Ghaziabad on the occasion Pharmacovigilance Week celebrated from September 17, 2022 to September 23, 2022 throughout the country. The Pharmacovigilance week was also celebrated with great zeal at our institute which is a designated ADR monitoring centre. The winning poster and snippets of the celebration have also been shared here.

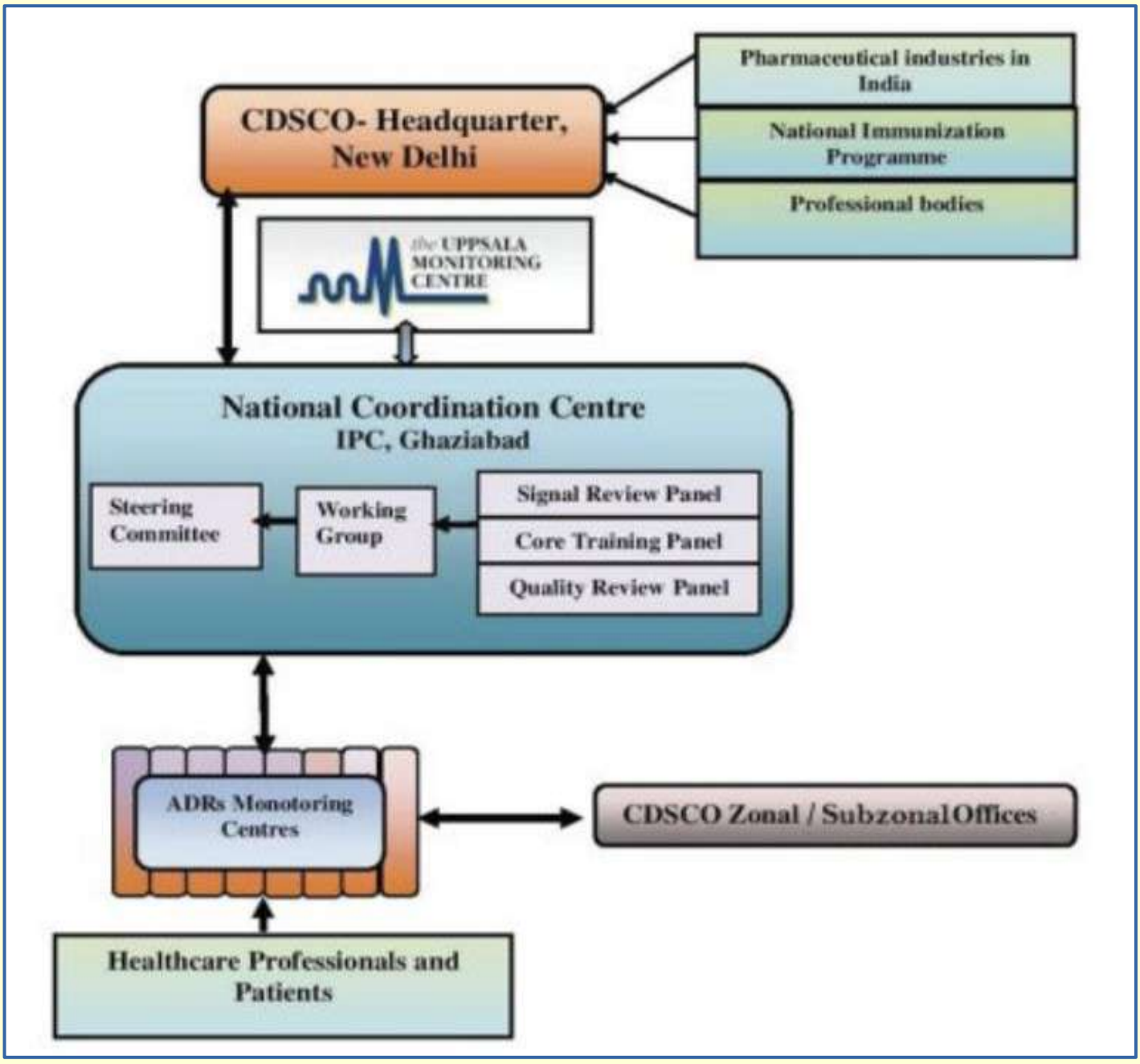
Hope you all shall enjoy reading this compilation.

Pharmacovigilance Program of India

The Pharmacovigilance Program of India (PvPI) was started in July 2010 by Ministry of Health and Family Welfare, Govt. of India with the vision to improve patient safety and welfare in the Indian population by monitoring drug safety and thereby reducing the risk associated with use of medicines.

Indian Pharmacopoeia Commission (IPC), Ghaziabad is the National Coordination Centre (NCC) for PvPI. WHO on 30th October, 2017 recognized IPC-PvPI as a WHO-Collaborating Centre for Pharmacovigilance in public health programmes and regulatory services. PvPI has collaborated with several national health programmes and research institutions.

To monitor Adverse Drug Reactions (ADRs), ADR Monitoring Centre (AMC), have been set up all over India, which send reports to NCC. The NCC-PvPI collects, collates and evaluates spontaneous ADR reports from the AMCs which are reported by health care professionals (HCPs) and consumers/ patients.



Currently there are 606 AMCs across the country which include various medical colleges. Our Institute, Dr.RMLIMS, Lucknow is one such AMC under PvPI. Dr. Atul Jain, Professor & Head, Department of Pharmacology is the coordinator of our AMC.

Communicating safety information to patients and HCPs is a public health responsibility borne by PvPI. Till date, several specific drug safety alerts/ signals have been identified and communicated to the HCPs and regulatory authority – CDSCO, for taking appropriate regulatory actions.

What to report?

All adverse events should be reported. Report serious or non-serious, known or unknown, frequent or rare adverse drug reactions due to Medicines, Vaccines & Herbal Products. A reaction is serious when the patient outcome is:

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability (significant, persistent or permanent)
- Congenital anomaly

Who can report?

All healthcare professionals (Clinicians, Dentists, Pharmacists and Nurse etc.) can report adverse drug reactions.

Where to report?

Duly filled in Suspected Adverse Drug Reaction Reporting Form can be sent to the nearest Adverse Drug Reaction Monitoring Centre (AMC) or directly to the National Coordination Centre (NCC) for PvPI.

Call on Helpline (Toll Free) 1800 180 3024 to report ADRs or directly mail the filled form to pvpi.ipc@gov.in

What happens to the submitted information?

Information provided in this form is handled in strict confidence. The causality assessment is carried out at AMCs by using WHO-UMC scale. The analysed forms are forwarded to the NCC-PvPI through ADR database. Finally, the data is analysed and forwarded to the Global Pharmacovigilance Database managed by WHO Uppsala Monitoring Centre in Sweden.

The reports are periodically reviewed by the NCC-PvPI. The information generated on the basis of these reports helps in continuous assessment of the benefit-risk ratio of medicines.

The information is submitted to the steering committee of PvPI constituted by ministry of health and family welfare. This committee reviews the data and suggests any intervention that is required such as restricted use of drug, change in label of drug, any precaution to be added or in extreme case drug may be even banned. After that regulatory authorities send advisories by circulating newsletter, drug alert and other related information to medical professionals for awareness and necessary action at their level.

For reporting ADRs at Dr.RMLIMS, contact Pharmacovigilance associate, **Mr. Anoop Kumar**, appointed in the Department of Pharmacology under Pharmacovigilance Programme of India by Indian Pharmacopoeia Commission, Ghaziabad

Mobile no: 9415266646 **Email:** anoop_singh72@yahoo.com

Version 1.4

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For **VOLUNTARY** reporting of ADRs by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION (National Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002

PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial Case ❑ | Follow-up Case ❑

FOR AMC / NCC USE ONLY

A. PATIENT INFORMATION *

1. Patient Initials:
2. Age or date of birth:
3. Gender: M ☐ F ☐ Other ☐
4. Weight (in Kg.)

B. SUSPECTED ADVERSE REACTION *

5. Event / Reaction start date (dd/mm/yyyy)
6. Event / Reaction stop date (dd/mm/yyyy)
7. Describe Event/Reaction management with details , if any

Reg. No. / IPD No. / OPD No. / CR No. :

AMC Report No. :

Worldwide Unique No. :

12. Relevant investigations with dates :

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

14. Seriousness of the reaction : No ☐ if Yes ☐ *(please tick anyone)*

☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly
☐ Life threatening ☐ Disability
☐ Hospitalization-Initial/Prolonged ☐ Other Medically important

15. Outcome:

☐ Recovered ☐ Recovering ☐ Not Recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S) *

S. No.	8. Name (Brand/ Generic)	Manufacturer (if known)	Batch No. / Lot No.	Expiry Date (if known)	Dose	Route	Frequency	Therapy Dates: Date Started	Therapy Dates: Date Stopped	Indication	Causality Assessment
i											
ii											
iii											
iv#											

9. Action taken after reaction *(please tick)*

S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown
i						
ii						
iii						
iv						

10. Reaction reappeared after reintroduction of suspected medication *(please tick)*

Yes	No	Effect unknown	Dose (if re-introduced)

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates: Date Started	Therapy Dates: Date Stopped	Indication
i							
ii							
iii#							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : _____

_____

Pin : _____ Email : _____

Contact No- : _____

Occupation : _____ Signature : _____

17. Date of this report (dd/mm/yyyy) :

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

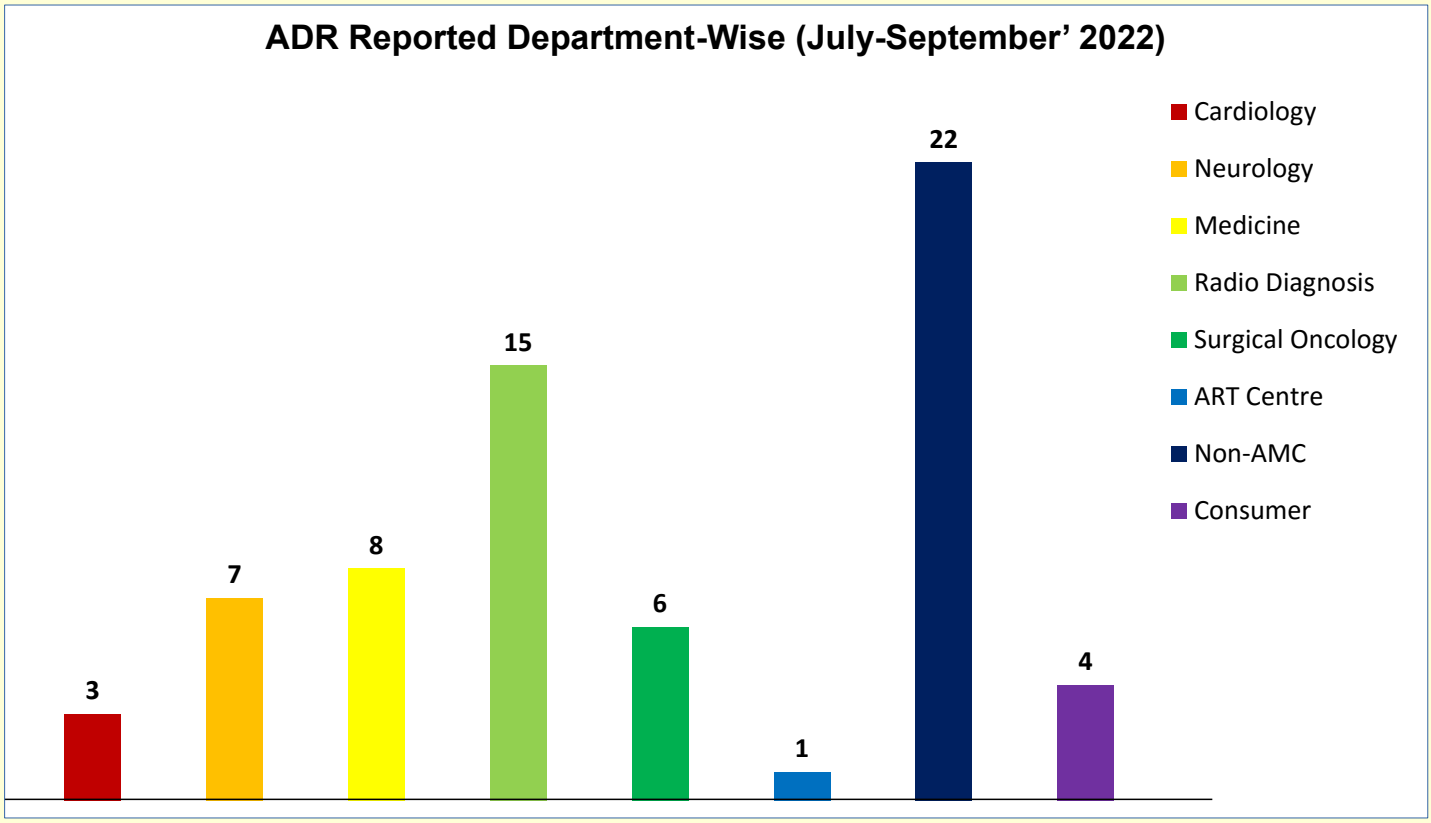
Use separate page for more information

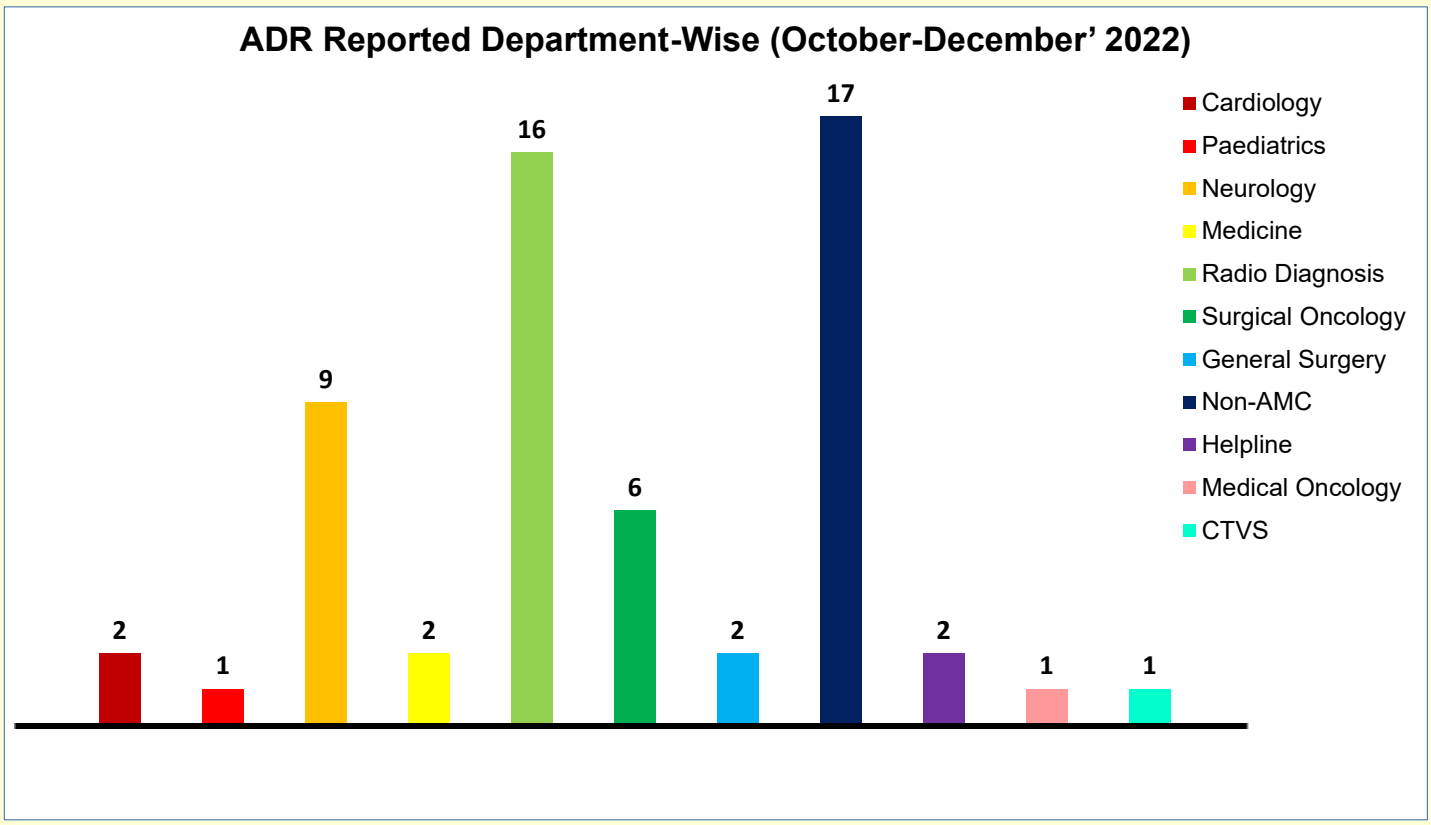
* Mandatory Fields for suspected ADR Reporting Form

Courtesy: www.ipc.gov.in

Mandatory fields for suspected ADR Reporting Form (*) Patient initials, age at onset of reaction, reaction term(s), date of onset of reaction, suspected medication(s) & reporter information.

ADRs reported by various departments of Dr. RMLIMS, Lucknow





Drug Safety Alerts

S.No.	Suspected Drugs	Indications	Adverse Drug Reactions
1.	Cefuroxime	• Indicated for lower and upper respiratory tract infection, urinary tract infection, gynaecological infection, skin or soft tissue infection etc	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
2.	Itraconazole	• Systemic aspergillosis, candidiasis, cryptococcus, sporotrichosis, paracoccidiomycosis, blastomycosis, other rarely occurring systemic or tropical mycoses • Empirical therapy of febrile neutropenic patients with suspected fungal infections	Symmetrical Drug Related – Intertriginous and Flexural Exanthema (SDRIFE)
3.	Trimetazidine	• Ischaemic heart disease, angina pectoris, sequelae of infarction and intermittent claudication	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
4.	Tacrolimus	• Prophylaxis of transplant rejection in kidney,lung, liver or heart allograft recipient • Treatment of allograft rejection resistant to treatment with other immuno- suppressive medicinal products • Treatment of patients with moderate to severe atopic dermatitis in whom the use of alternative conventional therapy is advisable	Gingival Hypertrophy
5.	Cefoperazone	• Urinary tract infections, biliary tract infections, respiratorytract infections, infections of skin tissues, meningitis, septicaemia	Coagulopathy
6.	Piroxicam	• Treatment of rheumatoid arthritis, osteoarthritis,acute gout,pain after operative intervention following acute trauma,primay dysmenorrhoea, ankylosing spondylitis, cervical spondylitis and other musculoskeletal disorder	Fixed Drug Eruption

Reference:

https://www.ipc.gov.in/ Assessed on 19th January-2022
Each Drug's hyperlink to be accessed via link given above

US-FDA Approved New Drugs (July-Dec 2022)

S.No.	Drug	Mechanism of Action	Indication	Date of Approval
1	Ublituximab-xiiy	It binds to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, it results in cell lysis through mechanisms including antibody-dependent cellular cytolysis and complement-dependent cytolysis	To treat relapsing forms of multiple sclerosis	28-12-2022
2	Anacaulase-bcdb	It is an enzyme which works by targeting and dissolving dead tissue. It will not damage any healthy skin as the enzyme only targets dead tissue	To remove eschar in adults with deep partial thickness or full thickness thermal burns	28-12-2022
3	Mosunetuzumab-axgb	It is a T-cell engaging bispecific antibody that binds to the CD3 receptor expressed on the surface of T-cells and CD20 expressed on the surface of lymphoma cells and some healthy B-lineage cells	To treat adults with relapsed or refractory follicular lymphoma, a type of non-Hodgkin lymphoma	22-12-2022
4	Lenacapavir	It is a novel first in class multistage, selective inhibitor of HIV capsid protein	To treat adults with HIV whose HIV infections cannot be successfully treated with other available treatments due to resistance, intolerance, or safety considerations	22-12-2022
5	Adagrasib	It is an irreversible inhibitor of KRAS G12C that covalently binds to the mutant cysteine in KRAS G12C and locks the mutant KRAS protein in its inactive state that prevents downstream signaling without affecting wild-type KRAS protein. It inhibits tumor cell growth and viability in cells harboring KRAS G12C mutations and results in tumor regression	To treat KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer in adults who have received at least one prior systemic therapy	12-12-2022

S.No.	Drug	Mechanism of Action	Indication	Date of Approval
6	Olutasidenib	It is a small-molecule inhibitor of mutated isocitrate dehydrogenase-1 (IDH1). In patients with AML, susceptible IDH1 mutations are defined as those leading to increased levels of 2-hydroxyglutarate (2-HG) in the leukemia cells	To treat adults with relapsed or refractory acute myeloid leukemia with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation	01-12-2022
7	Teplizumab-mzwv	It binds to CD3 (a cell surface antigen present on T lymphocytes) and delays the onset of Stage 3 type 1 diabetes in adults and pediatric patients aged 8 years and older with Stage 2 type 1 diabetes. The mechanism may involve partial agonistic signaling and deactivation of pancreatic beta cell autoreactive T lymphocytes	To delay the onset of stage 3 type 1 diabetes	18-11-2022
8	Mirvetuximab soravtansine-gynx	It is an antibody-drug conjugate (ADC). The antibody is a chimeric IgG1 directed against folate receptor alpha (FRα). The small molecule, DM4, is a microtubule inhibitor attached to the antibody via a cleavable linker. Upon binding to FRα, it is internalized followed by intracellular release of DM4 via proteolytic cleavage. DM4 disrupts the microtubule network within the cell, resulting in cell cycle arrest and apoptotic cell death	To treat patients with recurrent ovarian cancer resistant to platinum therapy	14-11-2022
9	Teclistamab-cqyv	It is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T-cells and B-cell maturation antigen (BCMA) expressed on the surface of multiple myeloma cells and some healthy B-lineage cells. Teclistamab-cqyv activated T-cells, caused the release of various proinflammatory cytokines, and resulted in the lysis of multiple myeloma cells	To treat relapsed or refractory multiple myeloma among adults who have received at least four specific lines of therapy	25-10-2022

S.No.	Drug	Mechanism of Action	Indication	Date of Approval
10	Tremelimumab-actl	CTLA-4 is a negative regulator of T-cell activity. Tremelimumab-actl is a monoclonal antibody that binds to CTLA-4 and blocks the interaction with its ligands CD80 and CD86, releasing CTLA-4-mediated inhibition of T-cell activation. It resulted in decreased tumor growth and increased proliferation of T cells in tumors	To treat unresectable hepatocellular carcinoma	21-10-2022
11	Futibatinib	It is a small molecule kinase inhibitor of FGFR 1, 2, 3, and 4 with IC50 values of less than 4 nM. It covalently binds FGFR. Constitutive FGFR signaling can support the proliferation and survival of malignant cells. Futibatinib inhibited FGFR phosphorylation and downstream signaling and decreased cell viability in cancer cell lines with FGFR alterations including FGFR fusions/rearrangements, amplifications, and mutations. Thus it demonstrates anti-tumor activity	To treat intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements	30-09-2022
12	Oomidenepag isopropyl ophthalmic solution	It is a relatively selective EP2 receptor agonist which decreases intraocular pressure (IOP)	To reduce elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension	22-09-2022
13	Terlipressin	It is a synthetic vasopressin analogue with twice the selectivity for vasopressin V1 receptors versus V2 receptors. It acts as both a prodrug for lysine-vasopressin, as well as having pharmacologic activity on its own. It is thought to increase renal blood flow in patients with hepatorenal syndrome by reducing portal hypertension and blood circulation in portal vessels and increasing effective arterial volume and mean arterial pressure (MAP)	To improve kidney function in adults with hepatorenal syndrome with rapid reduction in kidney function	14-09-2022

S.No.	Drug	Mechanism of Action	Indication	Date of Approval
14	Eflapegrastim	It is a recombinant human granulocyte growth factor that binds to G-CSF receptors on myeloid progenitor cells and neutrophils, triggering signaling pathways that control cell differentiation, proliferation, migration and survival	To decrease the incidence of infection in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia	09-09-2022
15	Deucravacitinib	It is an inhibitor of tyrosine kinase 2 (TYK2). It binds to the regulatory domain of TYK2, stabilizing an inhibitory interaction between the regulatory and the catalytic domains of the enzyme. This results in allosteric inhibition of receptor-mediated activation of TYK2	To treat moderate-to-severe plaque psoriasis	09-09-2022
16	DaxibotulinumtoxinA-lanm	It is a novel BoNTA product containing highly purified 150-kDa core neurotoxin and is the first to be formulated with a proprietary stabilizing excipient peptide (RTP004) instead of human serum albumin. The positively charged RTP004 has been shown to enhance binding of the neurotoxin to neuronal surfaces, which may enhance the likelihood of neurotoxin internalization	To treat moderate-to-severe glabellar lines associated with corrugator and/or procerus muscle activity for the management of glabellar rhytids	07-09-2022
17	Spesolimab	It is a humanized monoclonal immunoglobulin G1 antibody that inhibits IL-36 signaling by specifically binding to the IL36R which prevents the subsequent activation of IL36R by cognate ligands (IL-36 α, β and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways	For the treatment of generalized pustular psoriasis flares in adults	01-09-2022

S.No.	Drug	Mechanism of Action	Indication	Date of Approval
18	Olipudase alfa	It provides an exogenous source of enzyme acid sphingomyelinase (ASM). It is not expected to cross the blood-brain barrier or modulate the CNS manifestations of acid sphingomyelinase deficiency (ASMD)	For treatment of non–central nervous system manifestations of ASMD in adult and pediatric patients	31-08-2022

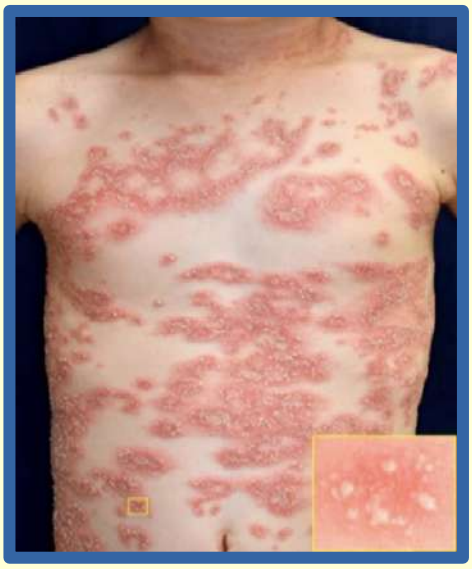
Reference:
https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2022 Accessed on January 19th, 2022
Each Drug's hyperlink to be accessed via link given above

Spesolimab

Generalized pustular psoriasis (GPP) is a rare, life-threatening neutrophilic skin disease, which is distinct from plaque psoriasis. It is characterized by episodes of widespread eruptions of painful, sterile pustules (blisters of non-infectious pus).

There is a high unmet need for treatments that can rapidly and completely resolve the symptoms of GPP flares. A person's quality of life is significantly impacted by flares, which can also result in hospitalization and potentially fatal complications such heart failure, renal failure, sepsis, and even death.

Interleukin-36 receptor antagonist Spesolimab, created in Chinese Hamster Ovary (CHO) cells using recombinant DNA technology, is a monoclonal IgG1 antibody (mAb) against human IL-36R.



The approval was based on data from the 12-week Effisayil 1 study (ClinicalTrials.gov Identifier: NCT03782792), which evaluated the safety and efficacy of spesolimab compared with placebo in patients with generalized pustular psoriasis presenting with an acute flare of moderate to severe intensity. Patients (mean age, 43; 32% men, 68% women) were randomly assigned to receive a single IV dose of spesolimab 900mg (n=35) or placebo (n=18) during the double-blind portion of the study. Results showed that a greater proportion of patients treated with spesolimab achieved a Generalised Pustular Psoriasis Physician Global Assessment Pustulation subscore of 0 at week 1 compared with placebo (54% vs 6%); risk difference vs placebo, 49% [95% CI, 21-67].[1]

Indications and usage: Treatment of generalized pustular psoriasis flares in adults.

Mechanism of Action: The precise mechanism between decreased IL36R activity and the treatment of flares of GPP is unclear. However, it has been discovered that by specifically interacting with the IL36R, it suppresses Interleukin-36 (IL-36) signalling. Subsequent activation of IL36R by cognate ligands (IL-36 α, β and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways are prevented by binding to IL36R.

Dosage forms: Colorless to slightly brownish-yellow, preservative-free, sterile solution.

Strengths: Injection: 450 mg/7.5 mL (60 mg/mL) solution in a single-dose vial.

Recommended Dose: Single 900 mg dose by intravenous infusion over 90 minutes.If GPP flares, an additional intravenous 900 mg dose (over 90 minutes) may be administered one week after the initial dose. [2]

Storage: Prior to use, may store unopened Spevigo vials at room temperature(20°C to 25°C) for up to 24 hours in the original carton to protect from light. Refrigerate the diluted solution at 2°C to 8°C

Adverse reactions

- Reduces the immune system's capacity to fight infections and may raise the risk of infection .
- Hypersensitivity and Infusion-Related Reactions: Includes immediate reactions such as anaphylaxis and delayed reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

Contraindications: Patients with severe or life-threatening hypersensitivity to Spesolimab or the excipients in present in it.

Warnings and precautions

Infections: Spesolimab is not recommended for use in patients with any clinically important active infection until the infection resolves or is adequately treated.

Tuberculosis: Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Spesolimab. Consider initiating anti-TB therapy prior to initiating Spesolimab in patients with latent TB or a history of TB in whom an adequate course of treatment cannot be confirmed. Avoid Spesolimab in patients with active TB infection.

Vaccinations: Avoid use of live vaccines in patients treated with Spesolimab.

Use in specific populations

Pregnancy: The data on the use of Spesolimab in pregnant women are insufficient to inform risk of adverse pregnancy-related outcomes.

Lactation: There are no data on the presence of Spesolimab in human milk, the effects on the breastfed infant, or the effects on milk production. Spesolimab is a monoclonal antibody and is expected to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Spesolimab and any potential adverse effects on the breastfed. [3]

Paediatrics: The safety and effectiveness of Spesolimab in paediatric patients have not been established.

References:

1. *EffisayilTM 1: A Study to Test Spesolimab (BI 655130) in Patients With a Flare-up of a Skin Disease Called Generalized Pustular Psoriasis - Full Text View - ClinicalTrials.gov [Internet]. [cited 2022 Sept 28]. Available from: https://www.clinicaltrials.gov/ct2/show/NCT03782792*
2. *FDA approves the first treatment option for generalized pustular psoriasis flares in adults. News release. Accessed September 2, 2022. https://www.prnewswire.com/news-releases/fda-approves-the-first-treatment-option-for-generalized-pustular-psoriasis-flares-in-adults-301616844.html*
3. *Spevigo. Package insert. Boehringer Ingelheim; 2022. Accessed September 2, 2022 https://docs.boehringeringelheim.com/Prescribing%20Information/PIs/Spevigo/Spevigo.pdf?DMW_FORMAT=pdf*

‘iNCOVACC’ - World’s first intra-nasal vaccine for COVID-19

‘ iNCOVACC’ the world’s first intra-nasal vaccine for COVID-19 is developed by India. It has got approval on 6th September 2022; from the Central Drugs Standard Control Organization (CDSCO) for restricted use in emergency situations. It is developed by Bharat Biotech International Limited (BBIL), supported by Department of Biotechnology (DBT) and, Biotechnology Industry Research Assistance Council (BIRAC) under the aegis of Mission COVID Suraksha. [1]

Route of Administration: It is delivered via the nose, from where the virus enters the body. It has the potential to block infection and break the cycle of transmission, as well as prevent lung damage. Its easy nasal delivery enables mass immunization to protect from emerging variants of concern.

Mechanism of Action: It is an intranasal replication-deficient chimpanzee adenovirus SARS-CoV-2 vectored vaccine. It consists of a replication deficient ChAd vector expressing the stabilized Spike SARS-CoV-2 (Wuhan variant).

SARS-CoV-2, the virus that causes COVID-19, uses a spike protein to invade cells. This spike protein was inserted into a adenovirus (a virus that causes the common cold). The adenovirus was tweaked, rendering it unable to cause illness. The harmless adenovirus carries the spike protein into the nose, enabling the body to mount an immune defense against the SARS-CoV-2 virus without becoming sick. The new vaccine also incorporates two mutations into the spike protein that stabilize it in a specific shape that is most conducive to forming antibodies against it. Additionally, adenovirus was genetically modified to improve production of the spike protein. Both innovations were designed to elicit a strong immune response. Thus, intranasal immunization of ChAd-SARS-CoV-2-S can create an immune response in the nose, which is the point of entry for the virus—thereby protecting against disease, infection, and transmission.

The design of the vaccine makes it relatively quick and easy to update when new variants emerge, simply by switching out the current spike protein with one from a new variant. So, it has benefit of enabling faster development of variant-specific vaccines. It promises to become an important tool in mass vaccinations during pandemics and endemics.

Preclinical and Clinical Studies:

In preclinical studies mice, hamsters and macaques were immunized with a single dose of ChAd-SARS-CoV-2-S conferred superior protection against SARS-CoV-2 challenge. Post-challenge with SARS-CoV-2, viral clearance was observed in both lower and upper airways in all these animal models.

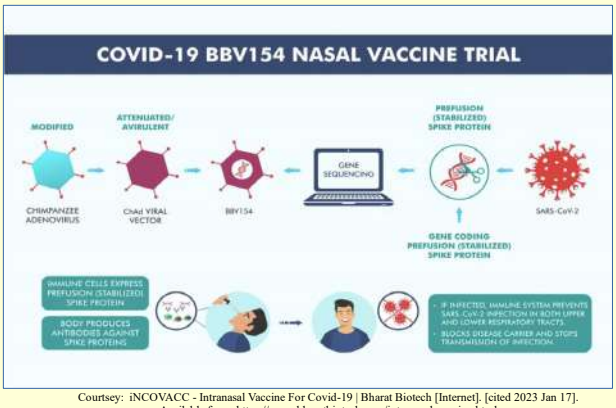
Phases I, II and III clinical trials were successful. Phase-III trials were conducted for safety, and immunogenicity in ~3100 subjects, in 14 trial sites across India (supported by BIRAC). Heterologous booster dose studies were conducted for safety and immunogenicity in ~875 subjects, where a booster dose (3rd dose) of BBV154 intranasal vaccine was administered to study participants who were previously vaccinated with licensed COVID vaccines.

These trials concluded that the vaccine is safe and effective in eliciting a strong immune response in people when used either as a primary vaccine or as a booster. Thus, vaccine has received emergency use authorization both as a primary vaccine as well as heterologous booster for those who received two doses of another COVID vaccine. [2,3]

Who should get: Approved for age ≥18 years

Who should not get: If you

- Had a severe allergic reaction to any ingredients of vaccine.
- Had a severe allergic reaction after a previous dose of this vaccine
- Currently have an acute infection or fever



Courtesy: iNCOVACC - Intranasal Vaccine For Covid-19 | Bharat Biotech [Internet]. [cited 2023 Jan 17]. Available from: https://www.bharatbiotech.com/intranasal-vaccine.html

Posology and method of administration

Primary Series: Two separate doses of 0.5mL (8 drops, 4 drops in each nostril). The second dose should be administered after 28 days (4 weeks from the first dose). Vaccine is stable at 2-8°C . [4]

Booster Dose: Indicated as a booster dose in individuals, at ≥6 months after completion of primary schedule of COVISHIELD or COVAXIN. [4]

Method of administration

- Blow nose gently to clear
- Tilt head back as far as comfortable
- Close one nostril with fore-finger
- Insert dropper a little away into another nostril
- Squeeze the dropper to release 4 drops and inhale gently
- Keep the head back for 30 seconds
- Repeat steps for another nostril

Side effects:

Systemic:

- **Common**: Fatigue, Fever, Headache
- **Uncommon:** Joint pain, Weakness, Cough, Cold, Itching in eyes, Redness in eyes, Breathlessness

Local:

- **Common**: Runny Nose
- **Uncommon:** Nasal Pain, Sneezing

Contraindications: Hypersensitivity to any constituents of the vaccine

Special warnings and precautions:

- Do not administer intramuscularly, intravenously, intradermally, or subcutaneously.
- Supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization.
- Vaccinees should remain under medical supervision for at least 30 minutes after vaccination.
- Concurrent illness: Administration of vaccine should be postponed in individuals suffering from an acute severe febrile illness/acute infection.
- Thrombocytopenia and coagulation disorders: Should be given with caution
- No data is available regarding its use in paediatric population, pregnant and lactating women.

References:

1. *World's first intra-nasal vaccine for COVID developed by India has got approval from the Central Drugs Standard Control Organisation (CDSCO) for restricted use in emergency situations in the age group of 18 and above. [Internet]. [cited 2023 Jan 17]. Available from: https://pib.gov.in/PressReleasePage.aspxPRID=1880328*
2. *Safety and Immunogenicity of an Intranasal SARS-CoV-2 Vaccine (BBV154) for COVID-19 - Full Text View - ClinicalTrials.gov [Internet]. [cited 2023 Jan 17]. Available from: https://clinicaltrials.gov/ct2/show/NCT04751682*
3. *Phase III Study of BBV154 Intranasal Vaccine in Healthy Volunteers - Full Text View - ClinicalTrials.gov [Internet]. [cited 2023 Jan 17]. Available from: https://clinicaltrials.gov/ct2/show/NCT05522335*
4. *iNCOVACC - Intranasal Vaccine For Covid-19 | Bharat Biotech [Internet]. [cited 2023 Jan 17]. Available from: https://www.bharatbiotech.com/intranasal-vaccine.html*

National Essential List of Medicine (NLEM) 2022

National Essential List of Medicine (NLEM) 2022 was released on 13 September 2022 in which 384 drugs across 27 therapeutic categories are included. [1] 34 medicines have been added to the list, while 26 drugs have been removed.

Popular antacid salt Ranitidine sold under the brand name Zantac has been deleted from the list. There was furore among the people that drug is been removed as it causes cancer. Standing National Committee on medicine and Health care product clarified that drug is not banned. It can be taken on the advice of doctor. It is removed from NLEM as government now has better option like Proton Pump Inhibitors, which are effective, safe and affordable.

Deletion from list had various reason like if there was non-availability, limited availability, non-essentiality in the present context and cost effectiveness. FDCs were not included, unless there is convincing evidence of therapeutic superiority over individual drugs.

Bleaching powder is removed as it is not used by clinicians and the fact that this can better fit into category of hygiene and healthcare products. Chlorpheniramine oral liquid 2 mg/5 ml formulation was removed by expert committee on the basis that it was not included in WHO EML 2019 and was not available in market. The literature review also suggested the superiority of cetirizine over other second generation. In view of the above, expert committee recommended chlorpheniramine oral liquid 2mg/5mL for deletion from list.

Erythromycin ointment 0.5% formulation was not available in market and expert committee noted that erythromycin is not superior to existing ophthalmic antibiotics. Therefore, it was deleted from the list. The basis of Ethinylestradiol 0.035mg + Norethisterone Tablet 1 mg removal was that it is not commonly prescribed and NLEM 2015 already has alternative combination of hormonal contraceptives Ethinylestradiol 0.03mg + Levonorgestrel 0.15mg which is commonly used.

Nicotinamide 50 mg was earlier included in the NLEM for the management of nutritional deficiency of Vitamin B3 - pellagra. Pellagra had almost disappeared due to public distribution system and no more a public health concern in India. In view of its limited utility, the expert group decided that formulation no longer meets the criteria for inclusion in the NLEM. So, it was decided to delete it from the revised list. [2]

Pentamidine Powder 200 mg for injection is no longer used for Kala-azar under NVBDCP. Therefore, the committee recommended its deletion in NLEM 2022. Stavudine 6mg + Lamivudine 30 mg Dispersible tablet has been removed as stavudine has been reported to be hepatotoxic therefore all formulations containing stavudine are deleted from NLEM, 2022.

This is the full list of medicines removed from the NLEM 2015: [3]

1. Alteplase	14. Lamivudine (A) + Nevirapine (B) + Stavudine (C)
2. Atenolol	15. Leflunomide
3. Bleaching Powder	16. Methyldopa
4. Capreomycin	17. Nicotinamide
5. Cetrimide	18. Pegylated interferon alfa 2a, Pegylated interferon alfa 2b
6. Chlorpheniramine	19. Pentamidine
7. Diloxanide furoate	20. Prilocaine (A) + Lignocaine (B)
8. Dimercaprol	21. Procarbazine
9. Erythromycin	22. Ranitidine
10. Ethinylestradiol	23. Rifabutin
11. Ethinylestradiol(A)+Norethisterone (B)	24. Stavudine (A) + Lamivudine (B)
12. Ganciclovir	25. Sucralfate
13. Kanamycin	26. White Petrolatum

Reference:
1. https://pib.gov.in/PressReleasePage.aspx?PRID=1858931. Accessed on January 15th, 2022
2. https://main.icmr.nic.in/sites/default/files/upload_documents/Report_and_NLEM_2022.pdf Accessed on January 15th, 2022
3. National List of Essential Medicines (NLEM), 2022 | Ministry of Health and Family Welfare | GOI [Internet]. [cited 2022 Nov 29]. Available from: https://main.mohfw.gov.in/newshighlights-104 Accessed on January 15th, 2022

Research Update: Antimicrobial Usage In India

Recently there has been a news article published in Times of India regarding the utilisation of antibiotics in India. The news article caused lot of furore in the general public due to it's headline " 44% of antibiotics consumed in India unapproved : Lancet". So, we thought of going deeper in the finding of the study that was quoted. The study mentioned was a cross-sectional study, analysing private-sector consumption of systemic antibiotics in India using the Defined Daily Dose (DDD) metrics and the WHO AWaRe classification system. It was published in Lancet Regional Health South East Asia.

The key findings of study:

- low per-capita consumption of antibiotics compared to previously reported rates
- high consumption rate of broad-spectrum antibiotics
- high consumption rate of FDCs discouraged by WHO
- large share of non-NLEM formulations in FDCs
- significant use of unapproved formulations

The research has found that Azithromycin 500mg tablet was the most consumed antibiotic formulation (7.6%) in India, followed by Cefixime 200 mg tablet (6.5%). It also shows that formulations listed in the NLEM contributed 49% while non listed formulations contribution was 51%. Single drug formulation sold were 66% and FDCs sold were 34%.

The study has revealed that over 47.1% of antibiotic formulations used in India's private sector in 2019 were not approved by the central drug regulator. Cephalosporins, Macrolides, and Penicillins were the top three antibiotic classes among unapproved formulations. More than 90% of Macrolides and 61% of Cephalosporins are sold in the market without the approval of the central agency.

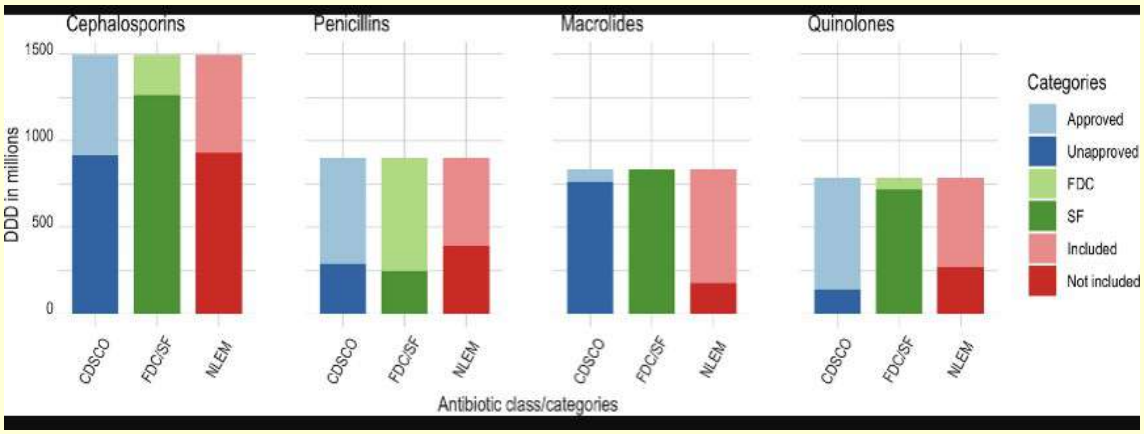


Fig 1: Characteristics of the top four antibiotic classes, 2019

The researchers found very high consumption of broad-spectrum antibiotics. Cephalosporins was on the top of list constituting 22.5% of usage. This may reflect inappropriate prescription or over-the-counter antibiotic dispensing and indicates the need for stricter regulations and stewardship programs. Researchers also found significant use of newer reserve antibiotics like Linezolid and Carbapenems.

It was also found in study that there was a lower consumption rate of antibiotics compared to previous estimates, it reflects a positive streak of light regarding antibiotic usage in India. This creates hope in us that with increase implementation of antibiotic stewardship program and public awareness about antibiotic use, one day India will surely land in positive framework of antibiotic usage. Thus, it will improve clinical outcome and minimum harm among patients.

Reference: *Koya SF, Ganesh S, Selvaraj S, Wirtz VJ, Galea S, Rockers PC. Consumption of systemic antibiotics in India in 2019. Lancet Reg Heal - Southeast Asia [Internet]. 2022 Sep 1 [cited 2022 Sep 12];4:100025. Available from:http://www.thelancet.co m/article/S2772368222000300/fulltext*

Glimpses of CME

"Current Perspectives on Pharmacovigilance: Present Scenario & Future Challenges"

Organised by Department of Pharmacology, Dr.RMLIMS, Lucknow

Under the aegis of Pharmacovigilance Programme of India (PvPI),

Indian Pharmacopoeia Commission, MoHFW, Govt. of India

06 August 2022

Inaugural ceremony

PG Quiz Competition

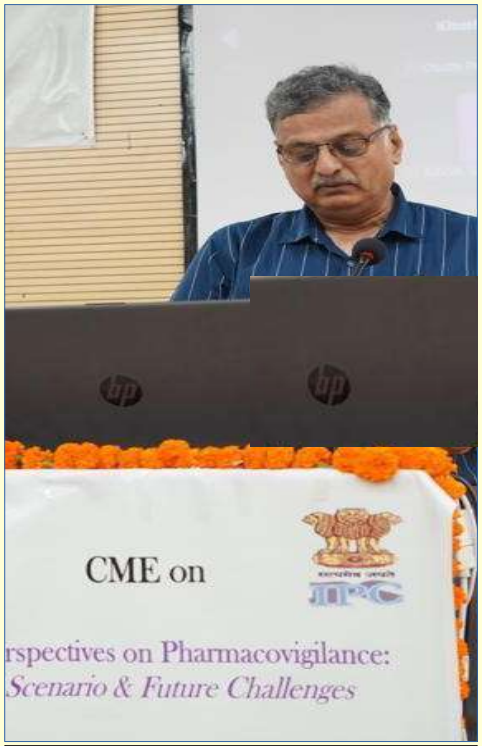
Poster competition

Speakers of the CME

Dr. Rakesh Kumar Dixit
Professor, Pharmacology
KGMU, Lucknow
(GUEST SPEAKER)

Dr. Dinesh Badyal
Vice Principal (Medical Education)
Prof, Dept. Of Medical Education &
Pharmacology, CMC Ludhiana
(GUEST OF HONOUR)

Dr. Sarvesh Singh
Additional Professor, Pharmacology
KGMU, Lucknow
(GUEST SPEAKER)



Dr. Atul Jain
Professor & Head, Pharmacology
Dr. RMLIMS, Lucknow
(Organising Chairman)

Dr. Arpita Singh
Additional Professor, Pharmacology
Dr. RMLIMS, Lucknow
(Organising Secretary)

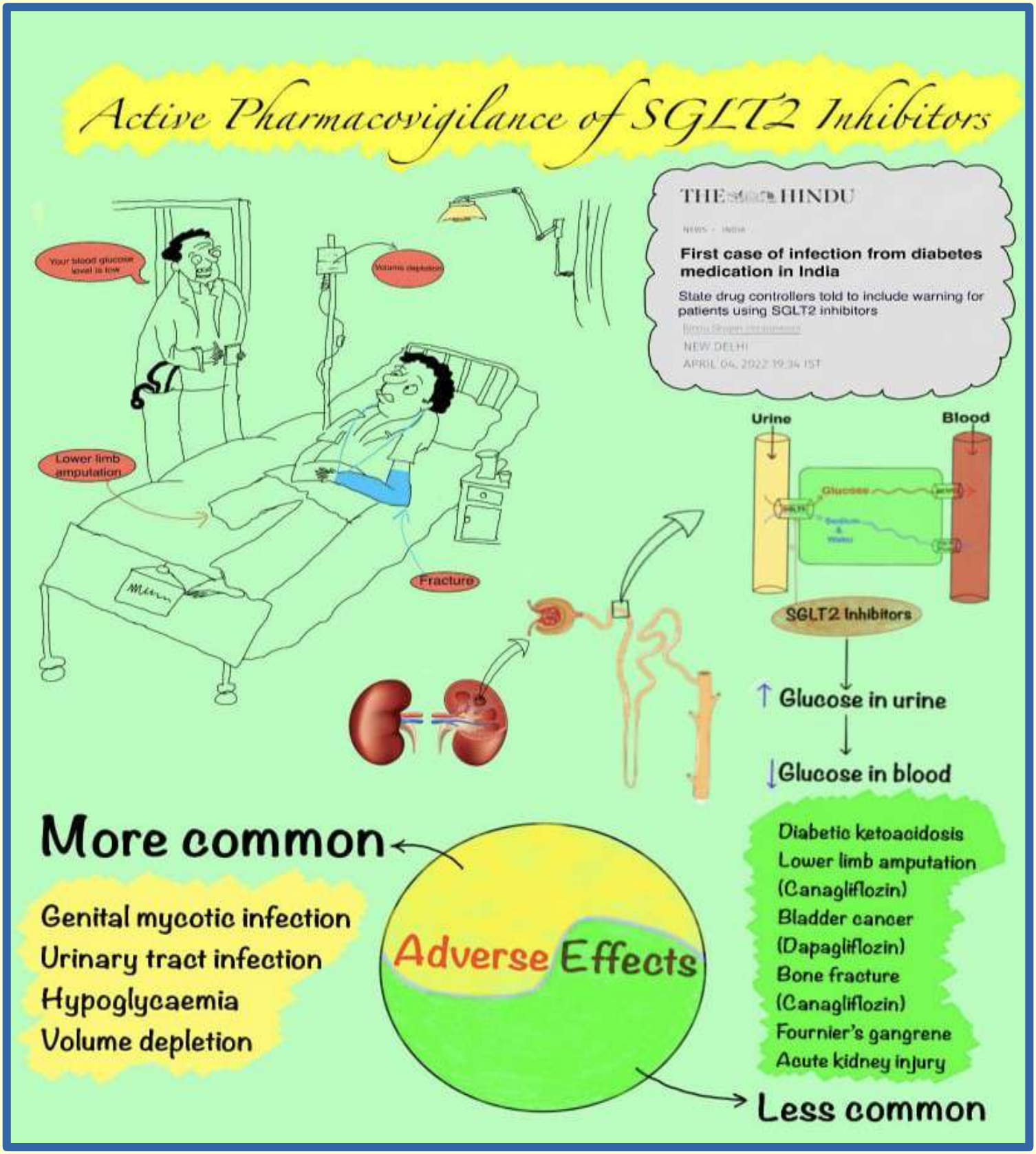
Glimpses of
National Pharmacovigilance Week Celebration
17th -23rd September 2022
Organised by ADR Monitoring Centre, Department of Pharmacology, Dr.RMLIMS, Lucknow

Sensitization lecture on pharmacovigilance and ADR reporting

Awareness Walk

Consumer /Patient sensitization for reporting ADRs

Felicitation of health care professionals for reporting ADRs



Junior residents (2021 Batch) from Department of Pharmacology, Dr.RMLIMS, Lucknow participated in National level poster competition on "Active Pharmacovigilance of SGLT2 Inhibitors" organised by Indian Pharmacovigilance Commission, Ghaziabad on the occasion of National Pharmacovigilance Week (17 to 24 September 2022) and won the Third Prize