

**Issue 13**

**August 2025**

# R<sub>x</sub> FACTOR

News letter by

**National Association of  
Pharmacology and Therapeutics**

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**National Association of  
Pharmacology and Therapeutics**

Promoting Pharmacology & Therapeutics for a better tomorrow

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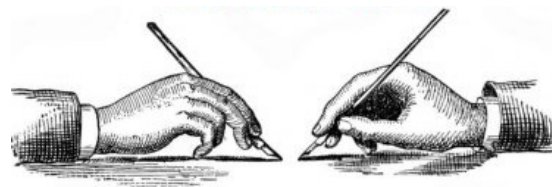
## Cool corner

Mini quiz, Puzzle, Cartoons, Mnemonics, images

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# Editorial

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Warm greetings to all.

Welcome to the Issue 12 of 'RxFactor', from the NATIONAL ASSOCIATION OF PHARMACOLOGY AND THERAPEUTICS (NPT). This issue continues to showcase the dynamic scope of Pharmacology and Therapeutics, encompassing developments in Medical Education, Pharmacovigilance, Research, and Clinical Practice.

The response to prior editions has been overwhelmingly positive, and we remain grateful for the appreciation and support received from our readers. Your encouragement drives our commitment to delivering content that informs, inspires, and advances the field.

The featured Articles in this Issue like Cytisinicline – Diversifying Treatment Options for Smoking Cessation explores the emergence of cytisinicline as a novel pharmacotherapeutic agent. We have a comprehensive overview bridging the chemical basis of beta-lactam allergy with practical implications for clinical decision-making. A reflective piece examining the future trajectory of pharmacology in the context of technological advancement and evolving healthcare needs: Whither Pharmacology.

In the Vigilant corner we have showcased a Digital Adverse Drug Reaction Reporting Form (ADR Form) which highlights efforts to simplify and digitize ADR documentation, promoting timely and accurate reporting within healthcare systems. Followed by it is article which reviews recent literature associating GLP-1 receptor

agonists with ocular adverse effects, emphasizing the need for vigilance in clinical settings. Pharmacovigilance in Psychiatry: Bridging the Safety Gap, addresses under-recognized safety concerns in psychiatric pharmacotherapy.

We have an update on emerging therapies and shifts in treatment paradigms for glaucoma, with an emphasis on the Indian healthcare landscape. Other interesting additions are The Concept of Biased Agonism: One Receptor and New Class of Antibiotic Found in Soil Sample: Lariocidin.

Our Cool Corner presents Causality Assessment – Using Cartoons. An innovative and engaging approach to pharmacovigilance education that simplifies causality analysis through visual storytelling.

We extend our heartfelt thanks to all authors and contributors whose scholarly work forms the foundation of this issue. A special mention to our Postgraduate students, whose diligence and insights reflect their emerging leadership in the discipline.

We remain committed to advancing mutual learning and professional excellence through RxFactor. We hope you find this issue both informative and thought-provoking.

With best regards,

Editorial Team National Association of Pharmacology and Therapeutics (NPT)

# Cytisinicline

## Diversifying treatment options for smoking cessation

Smoking is one of the major causes of preventable morbidity and mortality worldwide, and is responsible for approximately 8 million deaths annually.<sup>(1)</sup> It is one of the leading causes of tobacco related diseases, not just restricted to the respiratory system, but extending beyond it. Pharmacotherapy plays a pivotal role and helps reduce cravings, ease nicotine withdrawal symptoms, and increase the possibility of successful smoking cessation. Behavioral therapy is a non-pharmacological approach that promotes cognitive behavioral therapy techniques. Combination therapy involves both behavioral and pharmacological approaches, such as counselling to quit smoking, along with medications.

While the US FDA has approved different pharmacological therapies for smoking cessation, their efficacy is moderate and limited by adverse effect profiles. In this context, cytisnicline is a promising alternative for smoking cessation, along with other established treatment options.

### **Cytisus laburnum**

Cytisinicline (also known as cytisine) is a plant-based alkaloid extracted from the seeds of the yellow acacia (**Cytisus laburnum**) (2), a European decorative shrub generally known as “golden rain.” It is chemically similar to nicotine and pharmacologically resembles varenicline, acting as a partial agonist of the alpha-4 beta-2 nicotinic acetylcholine receptor.

The National Institute for Health and Care Excellence (NICE) has updated its guidelines on smoking cessation and recommends cytisnicline as a newer drug for the treatment of adults wishing to quit smoking. Therefore, the treatment options for clinicians in the UK should be expanded.

NICE recommends like all pharmacotherapies for smoking cessation, cytisnicline should be prescribed as part of a comprehensive program that includes behavioral support. It is not advised for use in pregnant or lactating women or individuals below 18 or above 65 years of age.

Cytisinicline can cause nausea and insomnia slightly more frequently than placebo or nicotine replacement therapy (NRT), but these side effects are mostly mild and manageable. Symptoms such as nausea and headaches can be linked to nicotine withdrawal itself, making it difficult to determine which effects are caused by the treatment medication versus the quitting process itself.

One of the main reasons for choosing cytisnicline for smoking cessation is its affordability. It is much cheaper than other smoking cessation treatments currently available. Some studies have reported higher smoking cessation rates among individuals treated with cytisnicline than those treated with varenicline (3) or nicotine replacement therapy (4).



### **Key Findings from Clinical Trials ORCA-2 Trial (Phase 3, U.S.)**

In this randomized clinical trial, 810 adult smokers were enrolled. The findings indicated that both 6-week and 12-week courses of a new cytisnicline dosing regimen were more effective than a placebo. These regimens were well tolerated and resulted in significantly higher smoking abstinence rates compared to the placebo during the final 4 weeks of treatment and from the end of treatment to 24 weeks. The study also confirmed the excellent efficacy and tolerability of cytisnicline.<sup>(5)</sup>

ORCA-3 Trial (Phase 3, U.S.) The Phase 3 ORCA-3 trial involved 792 adult smokers and was conducted at 20 clinical trial sites across the U.S.. This study confirmed the results of ORCA-2, demonstrating that cytisinicline significantly decreased nicotine cravings and boosted quit rates. No serious adverse events related to the drug were observed. The NDA submission to the FDA is scheduled for June 2025.(6)

### **FDA approval status**

Achieve Life Sciences, Inc., a pharmaceutical company, has officially submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA). NDA submission is a major step forward in treating adults who indulge in tobacco smoking and provides a newer tool for healthcare professionals to aid in the fight against nicotine dependence.

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# Beta-Lactam Cross-Reactivity: From Chemistry to Clinical Practice

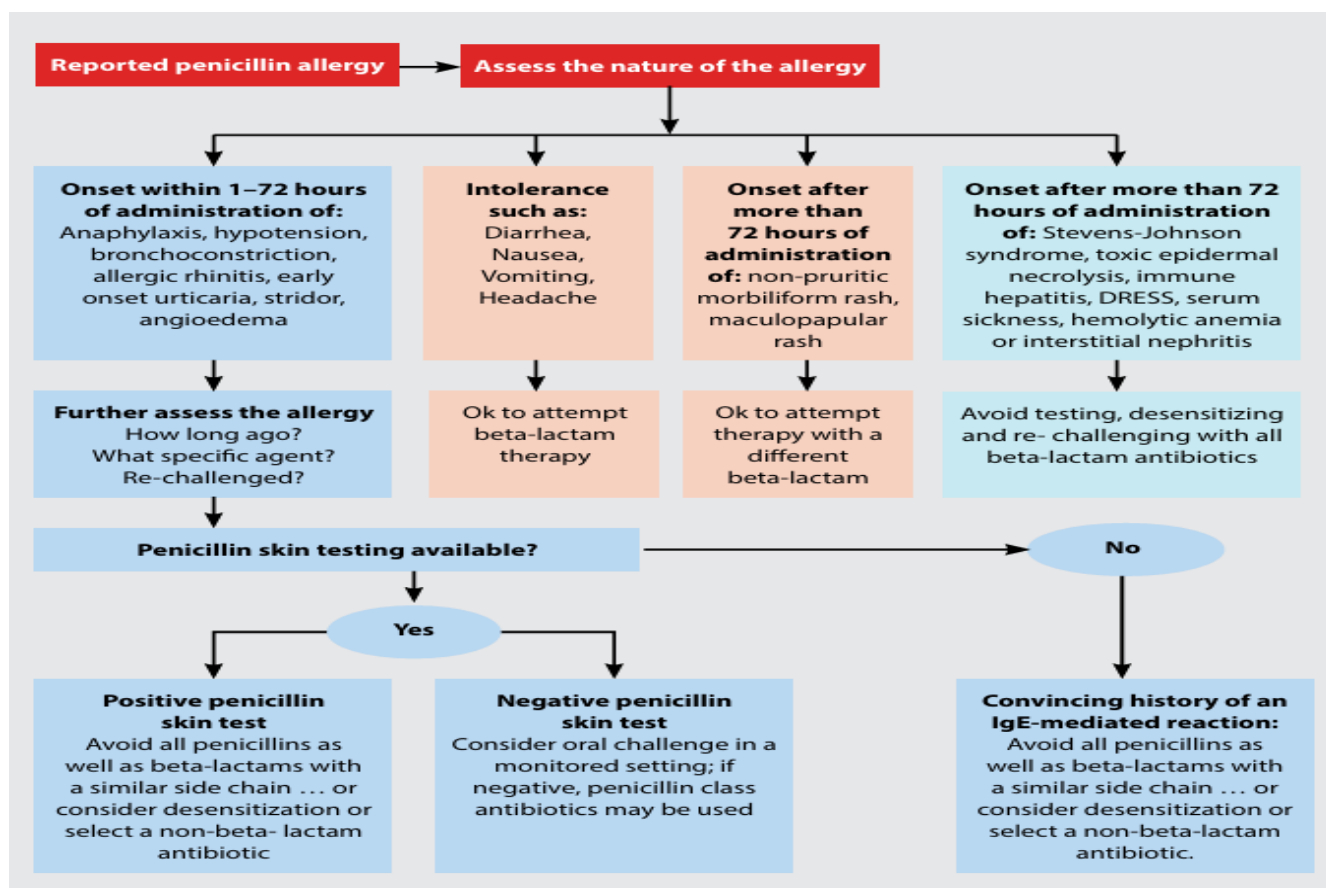
**Introduction** - Beta-lactam (BLM) antibiotics are the most commonly used antibiotics worldwide, including Penicillins, Cephalosporins, Monobactams, and Carbapenems. Despite their effectiveness, BLMs can cause adverse reactions, particularly allergic responses. The allergic responses are particularly concerning because of their potential severity and impact on outcomes. Patients with a reported BLM allergy are often prescribed alternative antibiotics which may be less effective, more costly, and contribute significantly to antimicrobial resistance.

**Understanding the Beta-Lactam Structure** - each class contain the Core  $\beta$ -lactam Ring along with side chains.

Class	Attached Ring Structure	Side Chains
Penicillins	5-membered <b>thiazolidine</b> ring (contains sulfur)	R
Cephalosporins	6-membered <b>dihydrothiazine</b> ring (contains sulfur)	R1 and R2

Carbapenems	5-membered ring with <b>carbon double bond</b> (no sulfur)	R
Monobactams	<b>No fused ring</b>	None or simple R

Cross-reactivity occurs when an individual is hypersensitive to a specific type of medication and develops hypersensitivity to other medications within the same family. Traditional clinical practice attributes BLM allergy to the commonality of beta-lactam ring, implying broad cross-reactivity between BLMs. But recently, it has been recognised that side chains contribute significantly to immunological recognition and thereby cross-reactivity due to side chain similarity. Cephalosporins have both R1 and R2 side chains, while Penicillin only have R1. Although the mechanisms of cross-reactivity may vary, it is primarily driven by similarities in the R1 side chains, with the highest risk occurring between BLMs that share identical side chains.



## Selecting Alternative $\beta$ -Lactams in $\beta$ -Lactam-Allergic Subjects

The best alternative BLM depends on the specific allergy, the type of reaction, and the clinical situation. The assessment of allergy enables classification of phenotypes as either severe versus non-severe and immediate versus delayed. This helps in stratifying the risk of using alternative BLM antibiotics.

In choosing an alternative  $\beta$ -lactam for a BLM allergic patient, it is important to consider its potential cross-reactivity to the responsible drug. The notion that penicillin-allergic patients must avoid all cephalosporins, or that a patient allergic to one cephalosporin must avoid all cephalosporins, due to potential cross-reactivity, should be dismissed as a

myth, as such cross-reactivity is primarily related to similarities in the side chains.

A matrix (Fig 2) summarizing **BLM Antibiotic Cross-Allergy Chart** visually represents the **likelihood of cross-reactivity** among various BLMs.

**AVOID ALL beta-lactam antibiotics if:**

- ICU admission related to allergy
- Delayed beta-lactam antibiotic allergy causing:
  - interstitial nephritis
  - hepatitis
  - hemolytic anemia
- Delayed severe skin allergic reactions:
  - Stevens-Johnson syndrome
  - toxic epidermal necrolysis
  - exfoliative dermatitis
  - acute generalized exanthematous pustulosis (AGEP)
  - drug reaction with eosinophilia and systemic symptoms (DRESS)

Expert-recommended comprehensive allergy assessments typically incorporate the administration of structurally dissimilar BLM antibiotics. For individuals with suspected allergy, cephalosporin and penicillin with similar side chains should be avoided, and those with dissimilar side chains

can be prescribed. For example, in a patient allergic to amoxicillin, Cefadroxil should be avoided due to an identical R1 side chain, whereas cefazolin

**Beta-lactam Antibiotic Cross-Allergy Chart**

Beta-lactams	AMOXICILLIN*	AMPICILLIN	CLOXACILLIN	PENICILLIN	PIPERACILLIN*	CEFADROXIL	CEFAZOLIN	CEPHALEXIN	CEFOXITIN	CEFPROZIL	CEFUROXIME	CEFIXIME	CEFOTAXIME	CEFTAZIDIME	CEFTRIAXONE	CEFEPIME	ERTAPENEM	IMIPENEM	MEROPENEM
AMOXICILLIN*		X <sup>1</sup>	X <sup>5</sup>	X <sup>4</sup>	X <sup>3</sup>	X <sup>1</sup>	✓	X <sup>1</sup>	✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
AMPICILLIN	X <sup>1</sup>		X <sup>5</sup>	X <sup>4</sup>	X <sup>3</sup>	X <sup>2</sup>	✓	X <sup>2</sup>	✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
CLOXACILLIN	X <sup>5</sup>	X <sup>5</sup>		X <sup>5</sup>	X <sup>5</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PENICILLIN	X <sup>4</sup>	X <sup>4</sup>	X <sup>5</sup>		X <sup>5</sup>	✓	✓	✓	X <sup>3</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PIPERACILLIN*	X <sup>3</sup>	X <sup>3</sup>	X <sup>5</sup>	X <sup>5</sup>		X <sup>3</sup>	✓	X <sup>3</sup>	✓	X <sup>3</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFADROXIL	X <sup>1</sup>	X <sup>2</sup>	✓	✓	X <sup>3</sup>		✓	X <sup>1</sup>	✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFAZOLIN	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEPHALEXIN	X <sup>1</sup>	X <sup>2</sup>	✓	✓	X <sup>3</sup>	X <sup>1</sup>	✓		✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFOXITIN	✓	✓	✓	X <sup>3</sup>	✓	✓	✓	✓		✓	X <sup>2</sup>	✓	✓	✓	✓	✓	✓	✓	✓
CEFPROZIL	X <sup>2</sup>	X <sup>2</sup>	✓	✓	X <sup>3</sup>	X <sup>2</sup>	✓	X <sup>2</sup>	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFUROXIME	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>2</sup>	✓		X <sup>3</sup>	X <sup>1</sup>	X <sup>3</sup>	X <sup>1</sup>	X <sup>2</sup>	✓	✓	✓
CEFIXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>3</sup>		X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	✓	✓	✓
CEFOTAXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>1</sup>	X <sup>3</sup>		X <sup>3</sup>	X <sup>1</sup>	X <sup>1</sup>	✓	✓	✓
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IMIPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>5</sup>		X <sup>5</sup>
MEROPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X <sup>5</sup>	X <sup>5</sup>	

\* Also applies to beta-lactamase inhibitor combinations (amoxicillin-clavulanate and piperacillin-tazobactam)

LEGEND:	
Penicillins	
1st Generation Cephalosporins	
2nd Generation Cephalosporins	
3rd Generation Cephalosporins	
4th Generation Cephalosporins	
Carbapenems	
✓	Different structure. <b>CONSIDERED SAFE TO PRESCRIBE</b>
<u>Reaction likely based on side chain:</u>	
X <sup>1</sup>	Same side chain - clinical evidence of cross reaction. <b>DO NOT PRESCRIBE</b>
X <sup>2</sup>	Same side chain - Theoretical risk of cross reaction, no clinical studies. <b>DO NOT PRESCRIBE</b>
X <sup>3</sup>	Similar side chain - Potential for cross reaction. <b>DO NOT PRESCRIBE</b>
<u>Reaction likely based on Beta-lactam ring</u>	
X <sup>4</sup>	Clinical evidence of cross reaction. <b>DO NOT PRESCRIBE</b>
X <sup>5</sup>	Theoretical risk of cross reaction, no clinical studies. <b>DO NOT PRESCRIBE</b>

may be considered, as it has a dissimilar side chain. Monobactams have no shared cross-reactivity with other beta-lactams, except Aztreonam, which shares an identical R1 side chain with ceftazidime. There is very low clinical cross reactivity between Carbapenems and beta-lactams.

In conclusion, clinically significant immunologically mediated cross-reactivity among  $\beta$ -lactams is

associated with R-group side chain homology, and  $\beta$ -lactam antibiotics with dissimilar side chains are thought to be associated with lower rates of cross-reactivity. Implementing a  $\beta$ -lactam side chain-based cross-reactivity chart, alongside enhanced allergy assessments, has been associated with safer and more frequent use of  $\beta$ -lactams—reducing reliance on broad-spectrum alternatives without increasing allergic reactions.

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# Whither Pharmacology??:

The pharmacology discipline is distressed today and the faculty is stressed! Lack of availability of adequately trained faculty and poor career choice for PG aspirants are important reasons. The pharmacology is conventionally considered as a *non-practicing para-clinical subject* and thus does not attract bright students to choose it as a career. In addition, there is paucity of psychomotor activity (experimental pharmacology is 'so passe') and greater passive learning during training period. Thus, lack of interest, complacency, diffidence and indifference percolate to erode his/her career as competent pharmacologist. This reverberates times and again. I am afraid, if this trend continues, and if we do not evolve and intervene, then, the discipline will be miniaturized or merged into general medicine. Teaching pharmacology in phase-II has done a further damage to subject resulting in loss of connectedness of discipline with clinical subjects. The much hyped 'integration' is rarely applied in organizing teaching of Phase-III subjects today. The UG students feel that pharmacology is boring isolated subject and they try to pass out anyway and forget it.

What roles can we play to restore the glory of subject and make it more relevant to clinics?

## Suggested Measures

**Splitting curriculum in two modules:** I feel pharmacology will become more relevant if efforts are made to split the curriculum training in two phases just as done in forensic medicine but in modular form

### Pharmacology Module-I (Phase-II)

**Course Contents:** General pharmacology, ANS, CNS, PNS, Autacoids, New drug development, chelating agents, immunomodulators, principles of management of poisoning, regulatory and legal framework, pharmacoeconomics and antimicrobials (excluding therapeutics). The skill sessions related to above sections also be conducted in Phase-II. The number of skill and theory hours shall be 50% (130 hrs) of the total curricular hours.

**Assessment:** The formative assessment may be done as per prescribed schedule and summative examination be conducted at the end of training of Phase-II, along with other phase-II subjects viz: pathology and microbiology. The theory examination would include Paper-I only of 100 marks and practicals 50 marks. The students who fail can also be permitted to continue phase-II part-I program and reappear after remediation.

### Pharmacology Module-II (Phase-III )

**Course Contents:** The remaining 50% teaching hours would include topics of systemic pharmacology

(Respiratory, CVS, Renal, Endocrine, blood and CHEMOTHERAPY) as per curriculum. The skill component would largely consist of prescription writing & audit, bedside therapeutic decision making (drug selection), critical appraisal of drug promotional literature, Interaction with industry representative, "communication exercises in Pharmacology" and ADR reporting (pharmacovigilance). The advantage of such division is that by the time students reach Phase-III (part-I and II), they have learnt principles of pharmacology and are already exposed to clinical teaching, thus, are poised for better learning. It will definitely be less stressful to learners (pharmacology is comparatively less comprehensible in bulk!).

## Assessment

The formative and summative assessment may be conducted in along with Phase-III (part-I) subjects. This would include theory Paper-II (100 marks) and practical examination (50 Marks).

The suggested modular format is a curricular *sea-change* and there will be many *ifs and buts*. A major difficulty would be to re-allocate 50% teaching hours of Phase-II (130 hrs) and add 50% of teaching hours in Phase-III (part-I). Some suggested modifications in curricular hours are-

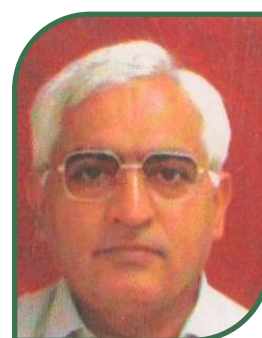
A: Reversal of forensic medicine to Phase-II only

B: Shifting teaching hours of minor clinical subjects (Anesthesiology, radiology and psychiatry) to Phase-II

C: Increasing Lecture hours of clinical subjects and increasing number of clinical posting hours in minor subjects in phase-II (thus reducing hours in Phase-III (part-I) to accommodate pharmacology)

Time is propitious to take remedial actions to revive pharmacology to a dignified level making

It relevant to present context lest it undergoes decay over coming decades!



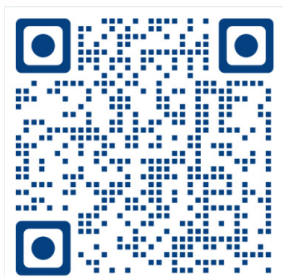
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# Digital Adverse Drug Reaction Reporting Form (ADR Form)

🔗 Try the Tool: <https://adrform-7b7ad.web.app>

📱 Scan QR to Access:



## 📌 What is ADR Form?

Digital ADR Form is a web-based application designed to simplify and encourage voluntary reporting of suspected adverse drug reactions (ADRs) by healthcare professionals. This tool promotes patient safety and helps build a stronger pharmacovigilance culture in clinical practice.

## 🎯 Purpose and Scope – Why Was This Created?

Feature	ADR Form	PvPI Mobile App
🎓 Target Audience	Faculty, students, residents, internal PvC teams	General public & healthcare professionals
🔗 Use Case	Training, simulation, internal audit, practice	Centralized national ADR reporting to IPC
🔄 Flexibility	Ideal for mock drills, offline case reviews	Strictly real-time reporting for national surveillance
🔒 Data Ownership	Full control remains with user	Data goes to IPC directly

## 🌟 Key Features That Set ADR Form Apart

### ✅ No Installation Required

Runs on any browser—no downloads, no updates, no device restrictions. Perfect for clinical rounds or classrooms.

### 🗣️ Voice Input Across All Fields

Use speech-to-text to fill the form—a major time-saver during busy hours.

### 🔗 Smart Templates for Common ADRs

Auto-suggested symptoms, drug names, and reactions. Minimize effort. Maximize accuracy.

### ⚙️ Dropdowns for Critical Fields

Make quick, error-free selections for:

- Route of Administration
- Causality Assessment
- Action Taken

### 🔒 Data Privacy by Design

No login required

No third-party tracking

Your data stays with you—perfect for institutional audits and mock simulations.

## 👤 Who Can Use This? – Real-World Scenarios

🏥 Doctors/Residents: Report new, severe, or rare ADRs on the go

🎓 Medical Colleges: Teach pharmacovigilance hands-on

💊 Pharmacists: Document suspected ADRs from prescriptions or walk-ins

📊 Researchers: Use the form for structured ADR trend analysis in projects

## 🔑 How to Use It in 5 Simple Steps

Visit <https://adrform-7b7ad.web.app>

Choose the case type – Initial or Follow-up

Fill each section using voice input or dropdowns

Preview, export, or share the form (PDF-ready)



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# Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) linked with Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Non-Arteritic anterior ischemic optic neuropathy (NAION) is defined by abrupt, painless, unilateral vision loss, typically linked to vascular risk factors and anatomical susceptibility. Recent evidence has associated Glucagon-Like Peptide-1 (GLP-1) receptor agonists, specifically Semaglutide (Ozempic) and Tirzepatide (Mounjaro), with an elevated risk of developing Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION). This relationship has substantial therapeutic ramifications owing to the prevalent utilization of these drugs for diabetes management and weight reduction. The European Medicines Agency (EMA) safety body, known as the Pharmacovigilance Risk Assessment Committee (PRAC), has recently determined that Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) is an exceedingly rare adverse effect of Semaglutide, potentially affecting up to 1 in 10,000 individuals using the medication.

## Clinical Evidence of GLP-1 Agonist Association

### Risk of NAION Associated with Semaglutide

The correlation between Semaglutide and NAION was initially documented by Hathaway et al. in 2024, who determined a hazard ratio of 4.28 (95% CI 1.62-11.29) for the onset of NAION within three years of commencing Semaglutide in a retrospective analysis of 710 patients with type 2 diabetes. This discovery necessitated further research into the correlation between GLP-1 receptor agonists and ocular neuropathy.

A robust Danish national cohort study conducted by Grauslund et al. revealed more substantial evidence by analysing 424,152 individuals with type 2 diabetes over a five-year period. The study stated that once-weekly Semaglutide more than doubled the risk of NAION (HR 2.19, 95% CI 1.54-3.12) in comparison to non-exposed individuals. This analysis identified epidemiological trends following the release of Semaglutide to the Danish market in November 2018, following which the incidence of NAION has increased exponentially.

## Tirzepatide and Non-Arteritic Anterior Ischemic Optic Neuropathy

Although comprehensive large-scale studies on Tirzepatide and NAION are scarce, case reports and clinical observations indicate a potential correlation. Tirzepatide, a dual agonist of Glucose-dependent Insulinotropic Polypeptide (GIP) and GLP-1 receptors, exhibits numerous pharmacological characteristics akin to Semaglutide and exhibits comparable cardiovascular and metabolic effects. The suggested mechanisms connecting GLP-1 agonists to NAION would potentially extend to Tirzepatide, although its dual receptor activation could modulate the risk profile.

## Proposed Mechanisms of Action

The precise mechanism by which GLP-1 agonists induce NAION remains ambiguous; nonetheless, certain aspects may be of importance:

### Anatomical Predisposition of “Disc at Risk”

NAION generally manifests in individuals possessing compact, congested optic discs, hence limiting their tolerance to ischemic injury. A case series by Hamid Ahmadi involving four patients treated with Semaglutide, who had small Bruch’s membrane apertures (< 1.4 mm) and optic nerve head crowding, indicated that Semaglutide may precipitate NAION in physically predisposed eyes.

### Direct Vascular Impacts

GLP-1 receptor expression has been detected in the optic nerve, suggesting potential direct vascular influences on circulation at the optic nerve head. GLP-1 agonists are known for inducing nitric oxide-mediated vasodilation, which may adversely affect perfusion of the optic nerve head.

### Accelerated Glycaemic Regulation and Early Worsening

The “early worsening” phenomenon of diabetic retinopathy with intensive glycaemic control is marked by a transient deterioration of retinal vascular disease during the initial year of treatment, contingent upon

the extent of HbA1c correction. The precise mechanism is unknown, but this swift metabolic alteration may exacerbate optic nerve head edema and venous congestion, particularly in crowded discs, leading to ischemia in vulnerable individuals.

### Management Strategies

Pre-treatment ophthalmological assessment.

Clinical monitoring during treatment.

Patient education regarding alarming signs and symptoms.

Halt therapy if NAION develops.

### Conclusion

Although the absolute possibility of developing NAION with GLP-1 receptor agonists is comparatively modest, the irreversible nature of visual loss associated with NAION requires meticulous patient selection, monitoring, and management measures. Clinicians must weigh the significant cardiovascular and metabolic advantages of these drugs against the risk of severe ophthalmological consequences, especially in patients with anatomical or systemic predispositions for NAION. With the increasing utilization of GLP-1

agonists, especially for weight control in non-diabetic populations, continuous monitoring for NAION and other possible consequences will be essential to ensure patient safety while keeping access to these advantageous treatments.

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# Pharmacovigilance in Psychiatry: Bridging the Safety Gap

In clinical psychiatry, one of the biggest hurdles we face is ensuring that the medicines we prescribe do more good than harm. Psychotropic drugs—especially antipsychotics and antidepressants—are central to treatment, but they often come with their own set of complications. From slurred speech to metabolic issues, adverse drug reactions (ADRs) remain a pressing challenge, affecting both compliance and patient trust.

In a recent study I conducted at J.L.N. Medical College & Hospital, Ajmer, we followed 105 psychiatric patients over six months to closely monitor the pattern and impact of ADRs. The numbers were striking: 264 ADRs were documented. Slurred speech emerged as a prevalent adverse drug reaction, reflecting potential central nervous system involvement in patients receiving psychotropic agents. (35.2%), rigidity (18.1%), and tremors (17.1%). Drugs like olanzapine and haloperidol were frequently implicated. Most patients received oral medications—primarily in tablet form—and twice-daily dosing was most common.

What made this study especially eye-opening was the effect these ADRs had on quality of life. Using the WHOQOL-BREF scale, we found that patients experiencing moderate to severe ADRs showed a significant decline in both physical and psychological well-being. While most ADRs were moderate (64.8%) or mild (35.2%), the cumulative toll on patients' daily lives was evident.

Interestingly, in more than 60% of the cases, treatment continued unchanged. However, about a quarter of

patients had to stop the medication altogether, and in 10% the dose was adjusted. These are not just numbers—they reflect real decisions doctors and patients make every day in the face of side effects.

Certain patterns stood out. Haloperidol was frequently associated with movement disorders, while olanzapine commonly led to weight gain and gastrointestinal issues. SSRIs such as fluoxetine and escitalopram were linked to restlessness and nausea. Identifying these trends early allows for more proactive prescription adjustments.

Empowering patients to actively participate in their treatment is equally important. Educating them about common side effects and encouraging open communication about any unusual symptoms can make a meaningful difference. When patients are informed and engaged, ADRs can be detected early, managed effectively, and sometimes even prevented. Creating this sense of shared responsibility is a key step toward safer psychiatric care.

The takeaway? ADR monitoring should never be a mere formality. It must be an integral part of everyday psychiatric practice. This study reaffirmed my belief that careful observation, timely reporting, and patient education can greatly reduce unnecessary suffering. For clinicians, vigilance regarding adverse effects is not just best practice—it's essential medicine.



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# Recent drug therapy in treatment of Glaucoma in India

Glaucoma is a major cause of irreversible blindness, with India's cases projected to reach 111.8 million by 2040. Its prevalence in India ranges from 2% to 13%. Although its exact cause remains unclear, intraocular pressure is the only modifiable risk factor. Medical therapy is the primary treatment approach and has seen significant advancements.

**Approval:** The Drug Controller General of India (DCGI) has approved the Ripasudil-Timolol combination on April 1<sup>st</sup> 2025. This dual-action eye drop aims to control intraocular pressure (IOP) by enhancing aqueous humour outflow (Ripasudil) and reducing its production (Timolol).

## Mechanism of action-

### 1. Ripasudil- Selective ROCK inhibitor

- **ROCK Inhibition:** Rho Kinases – family of protein kinases that mediate small GTPase response.
- **In eye ROCK particularly expressed in trabecular meshwork.** Here it promotes assembly of actin fibres and focal adhesion.
- **Inhibition of ROCK helps in increasing trabecular outflow facility.**
- **Cytoskeletal Changes:** By inhibiting ROCK, ripasudil induces changes in the cytoskeleton of cells in the trabecular meshwork and Schlemm's canal. This includes:
  1. Retraction and rounding of cell bodies
  2. Disruption of actin bundles
  3. Reduced compaction of trabecular meshwork tissue
- **Increased Aqueous Outflow:** These cytoskeletal changes result in increased outflow facility, allowing more aqueous humour to drain from the eye, thus reducing IOP.

**2. Timolol- Nonselective beta blocker [ beta 1 + beta 2].** Timolol, when applied topically, penetrates the eye and blocks beta-adrenergic receptors in the ciliary epithelium. This blockage leads to a decrease in the production of aqueous humor. Lowered IOP : By reducing the amount of aqueous humor produced, timolol effectively lowers the overall pressure within the eye, which is beneficial in glaucoma.

## Overall Advantages of the Combination:

- **Simplified Treatment:** A combination drop formulation can simplify the treatment regimen for patients, potentially improving adherence.
- **Potentially Better IOP Control:** The dual mechanism of action may lead to more effective and sustained IOP reduction compared to using either medication alone.

- **Potential for Delayed or Avoided Surgery:** By providing better IOP control, the combination may delay or prevent the need for glaucoma surgery.

## Recent advances in glaucoma treatment around the globe-

- **iDose® TR Implant:** The FDA recently approved the iDose® TR, a first-of-its-kind implant that delivers continuous drug therapy for up to three years. The implant, which releases travoprost intracameral, helps manage IOP in glaucoma patients, offering a long-term solution compared to traditional eye drops.
- **Genome- Wide Association Studies (GWAS):** A major GWAS identified 44 new gene loci associated with glaucoma and confirmed 83 previously known loci. This extensive study, which included a diverse population, could improve genetic testing and targeted treatments.
- **Gene Therapy:** Researchers at Trinity College Dublin have developed a groundbreaking gene therapy targeting the enzyme matrix metalloproteinase-3 (MMP-3). This innovative approach holds great promise in treating glaucoma by protecting and regenerating optic nerve cells, offering a hopeful glimpse into potential clinical applications.
- **New Medications:** The FDA's recent approval of Omlonti (omidenepag isopropyl), a new eye drop medication that enhances aqueous humor drainage through unique pharmacological actions, is a significant in patients with primary open-angle glaucoma.
- **Vision Restoration Initiatives:** The Catalyst for a Cure Vision Restoration Initiative focuses on regenerating the optic nerve's retinal ganglion cells and axons.
- These advancements highlight a multi-faceted approach to glaucoma treatment, from innovative drug delivery systems and genetic research to cutting-edge gene therapies and regenerative medicine, significantly improving prospects for those affected by this disease.



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# THE CONCEPT OF BIASED AGONISM: ONE RECEPTOR, MANY OUTCOMES

## Introduction

**Biased agonism**, also known as functional selectivity or ligand-directed signalling, is a revolutionary concept in pharmacology that has opened up new perspectives in therapeutic drug development. It is one of the fastest growing topics in G-Protein Couple Receptor (GPCR) Signalling that challenges the conventional view of interaction between ligand (drug) and the receptor.

The prevailing view was that a drug (agonist) activates all downstream signalling pathways of a receptor uniformly. As the name implies, biased agonism is when a ligand selectively activates one signalling pathway over another through the same receptor.

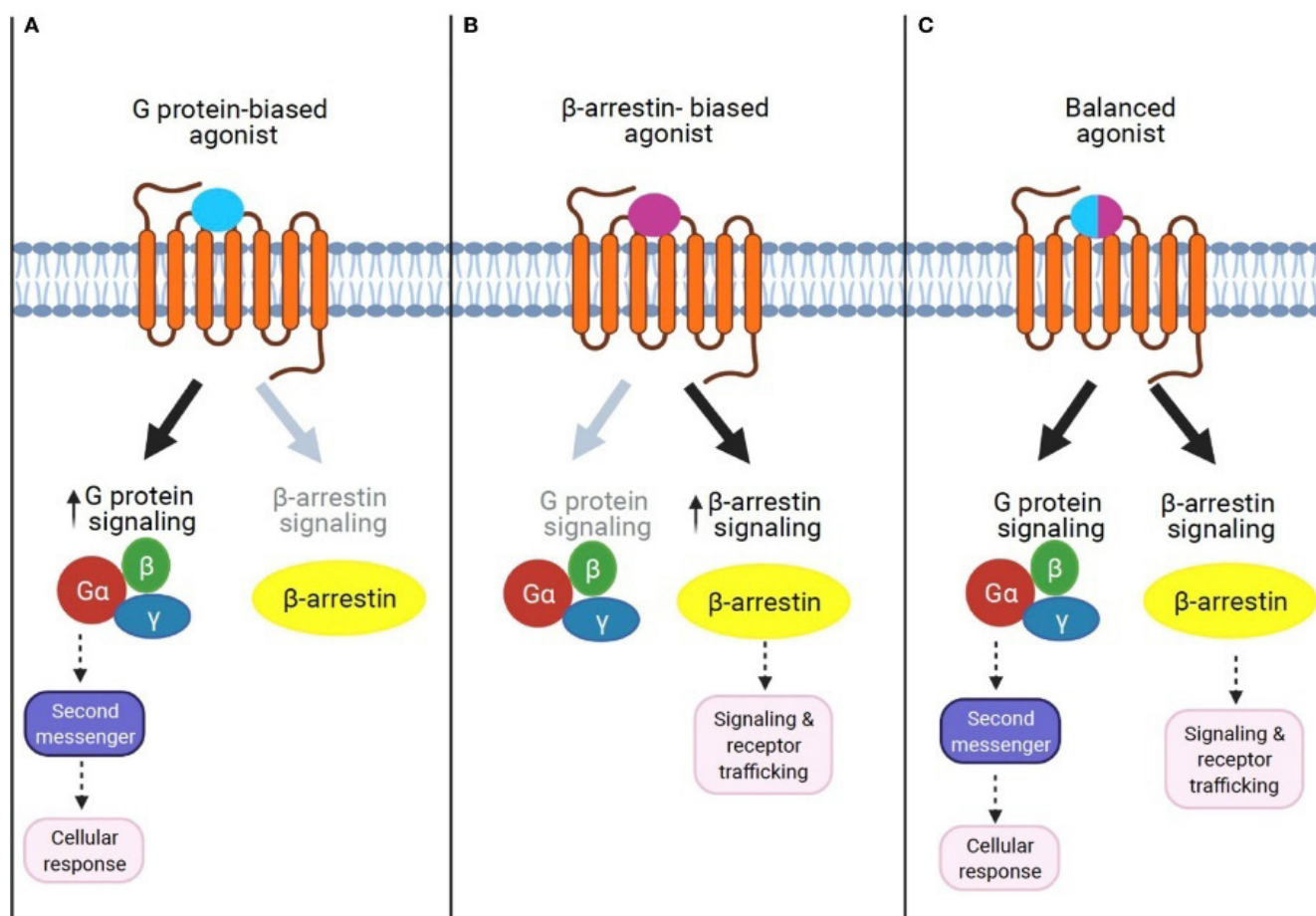
This signifies that different cellular responses can be produced from a single receptor depending on which ligand binds to it and which intracellular signalling

cascade it favors—typically G-protein vs  $\beta$ -arrestin pathways.

Drugs like Carvedilol marketed as third generation Beta blocker is later found to be a biased agonist of beta-adrenergic receptor is used in the clinic today. However, there is lesser understanding of biased agonism when compared to traditional pharmacology<sup>1</sup>. Thus, the development of biased agonists as drugs requires a detailed pharmacological and physiological characterization as they provide a novel mechanism for treating diseases<sup>2</sup>.

## Mechanistic basis of Biased Signalling<sup>3</sup>

GPCR mediated signalling is dependent on the conformation (3-Dimensional shape) of the receptor<sup>1</sup>. When a ligand binds to GPCR, it can differentially activate one of the above 3 signalling pathways i.e.,



G-protein,  $\beta$  arrestin (biased agonist) or both (balanced agonist) due to stabilization of distinct receptor conformational state<sup>2</sup>.

While the concept of  $G\alpha\beta\gamma$  Protein mediated signalling is widely studied,  $\beta$ -arrestin signalling pathway is less well understood. The conformational change of the receptor is identified by G-protein coupled Receptor Kinases (GRK) which phosphorylates GPCR at specific sites creating a 'barcode' that allows the recruitment of  $\beta$ -arrestin<sup>4</sup>. This leads to  $\beta$ -arrestin binding to the phosphorylated receptor resulting in activation of  $\beta$ -arrestin pathway in GPCR signalling. Its primary functions are:

**Desensitization<sup>5</sup>:** Binding of  $\beta$ -arrestin to phosphorylated GPCR uncouples the receptor from G-Protein, thus inhibiting G protein dependent signalling.

**Internalization<sup>5</sup>:** Promotes endocytosis of GPCR into clathrin-coated pits.

**Signal transduction (G-Protein independent)<sup>5</sup>:**  $\beta$ -arrestin serve as scaffold proteins that activate diverse pathways like MAP

Kinase activation, PI3K/Akt Pathway.

The significance of biased signalling is increasingly appreciated as signalling pathways become linked to normal physiology and pathophysiology<sup>6</sup>.  $\beta$ -arrestin dependent pathways are known to regulate cell

growth, apoptosis, immune modulation and even cancer progression.

## Therapeutic Applications<sup>7,8</sup>

see table below

## Challenges

A detailed structural understanding of drug-receptor interactions is required in order to utilize the biased agonist in therapeutics<sup>9</sup>. The complexity of the GPCR dynamics makes it difficult to identify the ligands that stabilize a specific signalling pathway. Accurate measurement of biased signalling requires validated assay. But various assays may produce conflicting results due to differential amplification of signalling pathways which becomes challenging to distinguish between ligand bias and system bias<sup>10</sup>.

To combat these limitations, choose assays with similar levels of amplification to mitigate the chance of system bias, use cells and test the effects of biased agonists in physiologically relevant conditions. Ensure that the bias persists over biologically relevant time scale by obtaining data at discrete time intervals<sup>2</sup>.

## Conclusion

Drug discovery of biased agonists is an active area of research which has exploded over the past 5 years<sup>2</sup>. Many biased agonists are already being prescribed to millions of people. Due to current clinical use of biased agonists, it is important for a broad understanding of signalling by biased agonists from the pharmacological to physiological level<sup>2</sup>. Overcoming the challenges

DRUG	TARGET	BIAS	CLINICAL RELEVANCE
<b>OLICERIDINE (TRV130), BUPRENORPHINE</b>	$\mu$ -Opioid receptor (MOR)	G-Protein biased agonist Minimal $\beta$ -arrestin recruitment	Analgesia Less Respiratory depression, tolerance, constipation
<b>CARVEDILOL</b>	$\beta$ 1-Adrenergic Receptor	$\beta$ -arrestin biased agonist	$\beta$ blockade (Blocks G-Protein signalling) Activates cardioprotective $\beta$ -arrestin pathways
<b>TRV027 (Phase II for Acute CHF)</b>	Angiotensin II type 1 receptor (AT1R)	$\beta$ -arrestin biased agonist	Promotes vasodilatation without G-protein mediated vasoconstriction
<b>ARIPIPRAZOLE</b>	D2 receptor	Activates G-protein signalling Inhibits $\beta$ -arrestin recruitment	Reduces internalization and desensitization of D2 Receptors with less Extra Pyramidal side effects
<b>PLERIXAFOR</b>	Chemokine receptor type 4 (CXCR4)	G-protein (Antagonist) $\beta$ -arrestin biased agonist	Hematopoietic stem cell mobilization in combination with G-CSF in patients with NHL, MM

is key to unlock the real-world potential of biased agonists as novel therapeutics to improve patient outcomes.

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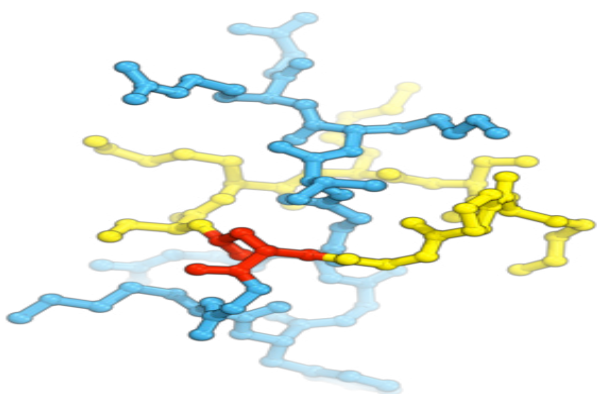
# New Class of Antibiotic Found in Soil

## Sample: Lariocidin

Antimicrobial resistance (AMR), particularly bacterial AMR, has now become a crucial global health threat, jeopardizing the efficacy of treatment and prevention of infections. With roughly 5 million deaths associated with bacterial AMR in 2019, this number is projected to increase substantially by 2050 if left unaddressed. Thus, urgent action is needed. New antibiotics that are safe and effective are very challenging to develop.

However, there is now some good news. Scientists have found a promising candidate that could eliminate even some of the toughest bacterial pathogens that now infect people and resist multiple drugs. This new candidate, named Lariocidin, was identified in a study published in the journal *Nature*.

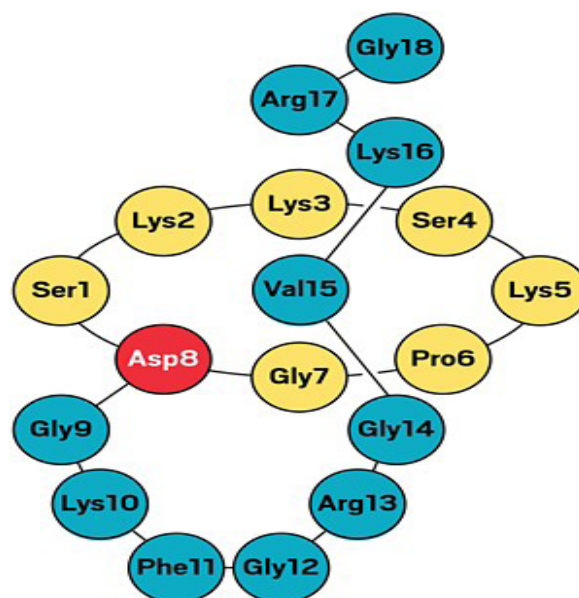
This new molecule is a kind of lasso peptide, and its mode of attack is unlike any other antibiotic. Lariocidin can directly attach to a complex that generates proteins in cells, called the ribosome, in a novel way. When it binds to the bacterial ribosome, protein synthesis is prevented, and bacterial cells cannot grow or survive without synthesizing proteins. "This is a new molecule with a new mode of action," said senior study author Gerry Wright, a professor at McMaster University, among other appointments. "It's a big leap forward for us."



Lariocidin, a lasso-shaped peptide with promising antibiotic properties, is made by bacteria known as *Paenibacillus*. In this case, the bacteria were collected from a soil sample taken from a backyard in Hamilton. The soil bacteria were grown for about a year, and during this time, the researchers found that *Paenibacillus* was

producing a compound with a strong effect on other bacteria, including those that are usually antibiotic resistant. The research team allowed the soil bacteria to grow in the lab for approximately one year—a method that helped reveal even the slow-growing species that could have otherwise been missed. One of these bacteria, *Paenibacillus*, was producing a new substance that had strong activity against other bacteria, including those typically resistant to antibiotics.

The peptide's unique structure may also help circumvent another common bacterial defense. To tie up a ribosome, an antibiotic first needs to get inside the bacterial cell. Many drugs sneak in through transporters, but bacteria can change or remove these to block the drugs. By contrast, Lariocidin has a strong positive charge, which likely allows it to pass directly through membranes without the need for transporters. That makes the molecule a broad-spectrum antibiotic.



Lariocidin is a lasso peptide containing an isopeptide bond at an aspartic acid residue and a tail that extends over and through a central ring structure. It exhibits broad-spectrum antibiotic activity and was effective at killing both gram-positive and gram-negative pathogenic bacteria, along with mycobacteria related to those that cause tuberculosis.

Lariocidin binds to the aminoacyl site in ribosomes. It is the acceptor site, where the new amino acid-containing transfer RNA binds. The ribosome can't read the codons in messenger RNA correctly, thus causing the mistranslation of proteins. It is a mode of action never before seen in an antimicrobial compound, and thus it is hopeful that Lariocidin could overcome antimicrobial resistance in a clinical setting.

Lariocidin not only kills bacteria; it also does not harm human cells. It was effective in an animal model of infection, and currently, it does not seem like microbes will easily become resistant to its effects.

Now, the researchers are working on methods to generate large amounts of this compound so that more work can be done to make an effective medication.

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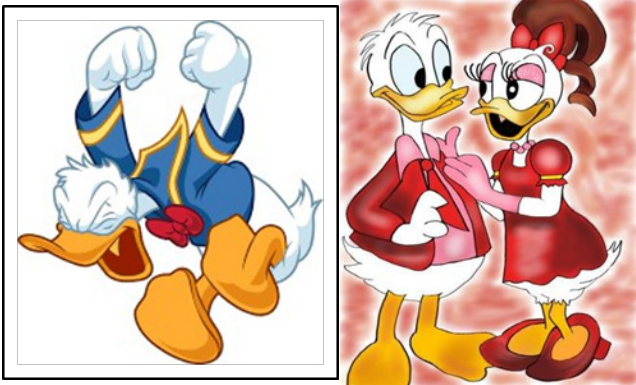
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# Causality Assessment Quiz– Using Cartoons



## 1.Characters: Mickey Mouse and Pluto

- Mickey Mouse starts taking a new medication for his allergies.
- After a few doses, he develops a severe rash and stops the medication.
- The rash disappears, and when he tries the medication again, the rash reappears.
- Pluto explains that this confirms the medication is causing the rash.
- Mickey decides to report this ADR to his doctor.

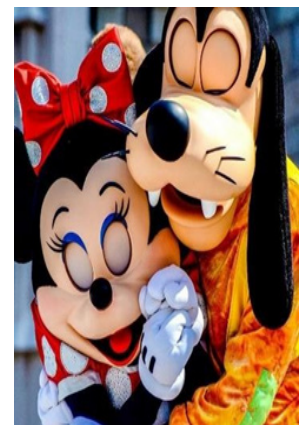


## 2.Characters: Donald Duck and Daisy Duck

- Donald Duck is taking medication for his arthritis.
- He starts feeling nauseous and suspects the new medication.
- When he stops taking it, the nausea goes away.
- Daisy tells him this is probably due to the medication since there's a strong temporal relationship.
- Donald discusses this ADR with his physician.

## 3.Characters: Minnie Mouse and Goofy

- Minnie Mouse begins a new medication for her headaches.
- She soon experiences dizziness but isn't sure if it's due to the medication or stress.
- She stops the medication, and the dizziness subsides, but it's inconclusive.
- Goofy suggests it could be a.....ADR since other factors could also be involved.
- Minnie decides to keep a symptom diary and consult her doctor.



## 4. Characters: Scrooge McDuck and Huey

- Scrooge McDuck takes a vitamin supplement and later feels fatigued.
- He wonders if the supplement is causing the fatigue.
- Huey points out that fatigue is not a common side effect of the supplement.
- They find out Scrooge has been overworking, which is a more likely cause.
- Scrooge realises this ADR is related to the supplement and takes a rest.

# Answer key of Causality Assessment Quiz

Here's the assessment of the causality of the adverse drug reactions (ADRs) in the provided stories using the WHO-UMC causality assessment scale:

## 1. Mickey Mouse and Pluto

WHO-UMC Assessment: Certain.

The strong temporal relationship, dechallenge (rash disappears on stopping the drug), and rechallenge (rash reappears on restarting the drug) strongly indicate a certain causal relationship.

## 2. Donald Duck and Daisy Duck

WHO-UMC Assessment: Probable/Likely.

There's a strong temporal relationship and a dechallenge, suggesting a probable/likely association between the medication and the nausea.

## 3. Minnie Mouse and Goofy

WHO-UMC Assessment: Possible.

While there's a temporal relationship and a dechallenge, the presence of other potential contributing factors (stress) makes the causality possible but not definitive.

## 4. Scrooge McDuck and Huey

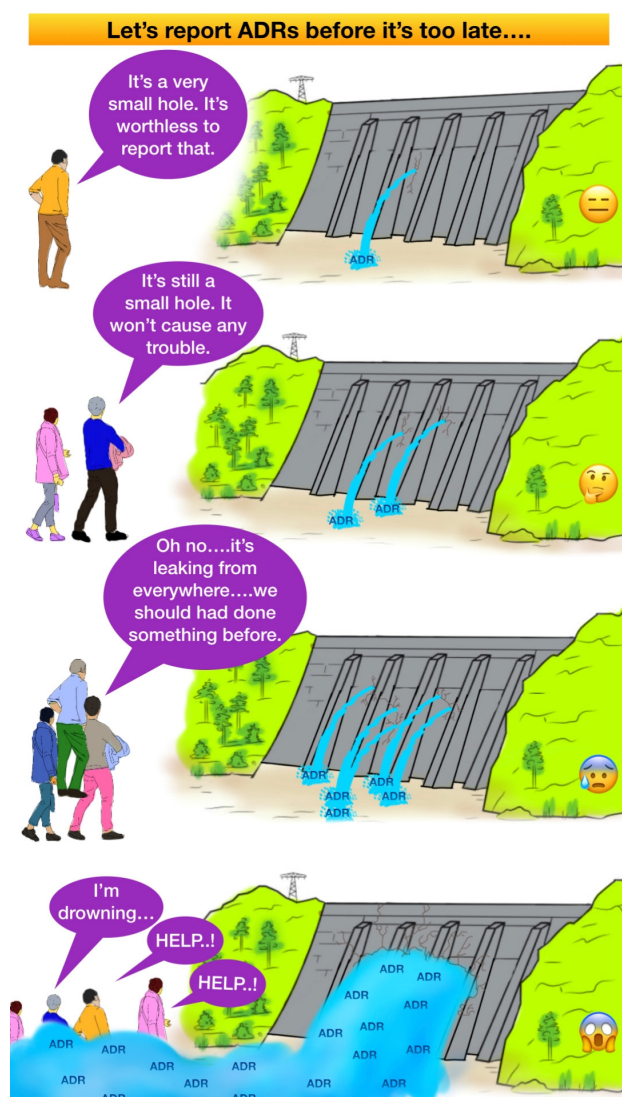
WHO-UMC Assessment: Unlikely.

Fatigue is not a typical side effect of the supplement, and another more plausible cause (overworking) is identified, making the association unlikely.



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It has been rightly said: "True prevention is not waiting for bad things to happen, it's preventing things from happening in the first place" - the same message is deployed in my illustration about ADR reporting. The person ignores the leaking water from the dam thinking it as a minor scratch. But more and more such leaks merged together making the dam to fall apart. Eventually the area is flooded and the people are drowned. The similar concept takes place in ignorance towards ADR reporting. People tend to ignore ADRs but eventually it gets accumulated and proves to be disastrous in the end."

# Advancements in SGLT2 Inhibitors: A Review of the Top 5 Trials in 2025

## INTRODUCTION:

SGLT2 inhibitors (sodium-glucose co-transporter 2 inhibitors) originally developed for type 2 diabetes mellitus (T2DM), they are now widely recognized for their cardiovascular and renal protective benefits. These drugs, including dapagliflozin, empagliflozin, and canagliflozin, reduce the risk of heart failure hospitalization and slow the progression of chronic kidney disease. They also promote weight loss and lower blood pressure. Recent studies have explored their potential benefits in conditions beyond diabetes, such as non-alcoholic fatty liver disease (NAFLD), Alzheimer's disease, and certain cancers. Following are the recent advances of SGLT2 inhibitors.

### 1. DAPAGLIFLOZIN IN RECURRENT ASCITES

This study explored whether dapagliflozin could similarly benefit patients with cirrhosis and recurrent ascites.

#### Study Design and Methods

This study was a double-blind, randomized controlled pilot trial involving 40 patients with cirrhosis and recurrent ascites. Participants were randomly assigned to one of two groups: Group A received dapagliflozin (10 mg/day) in addition to standard medical therapy, while Group B received a placebo alongside standard medical therapy. The primary outcome was the control of ascites at 6 months. Secondary outcomes included urine output, 24-hour urinary sodium, Child-Turcotte-Pugh (CTP) score, Model for End-Stage Liver Disease (MELD) score, survival at 6 months, and the incidence of acute kidney injury (AKI) and infections.

#### Conclusion

Dapagliflozin was found to improve the control of ascites and increase sodium excretion (natriuresis) in patients with cirrhosis. However, it did not lead to improvements in liver function scores or overall survival. The use of dapagliflozin was also associated with a higher risk of acute kidney injury (AKI) and infections. This study is registered under Clinical Trial Registration number NCT05014594.

### 2. CANAGLIFLOZIN REDUCES LUNG FIBROSIS IN LEFT HEART DYSFUNCTION

This study investigates the effect of canagliflozin on pulmonary fibrosis in a porcine model of chronic myocardial ischemia.

#### Methodology

Sixteen Yorkshire swine were randomized into two groups: control (normal diet, n = 8) and canagliflozin-treated (n = 8). All underwent left thoracotomy with placement of an ameroid constrictor on the left circumflex artery. After 7 weeks, heart function was assessed using pressure-volume loops, protein expression by immunoblotting, and collagen deposition by Masson's trichrome staining.

#### Conclusions

Canagliflozin may reduce chronic fibrotic changes in pulmonary hypertension secondary to left ventricular failure. Histological improvement in fibrosis showed a trend toward significance, possibly limited by the duration of the experimental model. Molecular findings suggest that canagliflozin modulates TGF $\beta$  signaling, potentially offering therapeutic benefits in secondary pulmonary hypertension.

### 3. DAPAGLIFLOZIN IN PTSD

This study investigates DAPA's effect on depressive-like behaviors using the single-prolonged stress (SPS) mouse model of PTSD.

#### Methods

Male mice were used in an animal model of stress by subjecting them to single prolonged stress (SPS), which included restraint, forced swim, rest, and ether exposure. The mice were divided into four groups (n = 4 each): a control group, an SPS group, a DAPA group (treated with dapagliflozin at 1 mg/kg/day orally for 7 days), and an SPS + DAPA group. Behavioral assessments included the Forced Swim Test (FST) and Tail Suspension Test (TST). Blood and brain tissues were collected to analyze stress markers and mRNA expression levels of Crh, Bax, Il1b, Bdnf, and serum corticosterone.

## Conclusion

Dapagliflozin (1 mg/kg) effectively reduces depressive-like behaviors induced by PTSD in mice. Its therapeutic effects are linked to the modulation of stress-related molecular and hormonal markers. These findings suggest that dapagliflozin may have potential as a treatment for PTSD beyond its current use for metabolic conditions.

## 4. SGLT2 INHIBITORS IN PARKINSON DISEASE

This study presents the **first large-scale, real-world, head-to-head comparison** of SGLT2is and metformin on the risk of developing PD in T2DM patients.

## Methods

Data for this study were obtained from the TriNetX platform (2005–2025), which includes information from 142 healthcare organizations. The population consisted of 913,428 patients with type 2 diabetes mellitus (T2DM), including 96,018 users of SGLT2 inhibitors and 817,410 users of metformin. Patients with prior Parkinson's disease (PD), other neurodegenerative diseases, or those using neuroprotective or neurotoxic antidiabetic drugs were excluded. A 1:1 propensity score matching was performed to balance demographic, clinical, and pharmacological variables between groups. The analysis used a Cox proportional hazards model to estimate adjusted hazard ratios (aHRs), which were validated with positive controls (dementia) and negative controls.

## Conclusions

SGLT2 inhibitors may provide better neuroprotection against Parkinson's disease compared to metformin in patients with type 2 diabetes mellitus. The study's robust design and use of controls support this association. These findings warrant further prospective research to confirm the neuroprotective potential of SGLT2 inhibitors, especially in diabetic patients at risk of neurodegeneration.

## 5. DAPAGLIFLOZIN IN DIABETIC PERIPHERAL NEUROPATHY

This study evaluated the effect of dapagliflozin, a sodium-glucose cotransporter-2 inhibitor (SGLT2i), on nerve regeneration and oxidative stress in patients with type 2 diabetes mellitus (T2DM) and DPN.

## Research Design and Methods

This prospective, open-label, randomized controlled

trial included 40 patients with type 2 diabetes and diabetic peripheral neuropathy. Group A (n = 22) received 10 mg/day dapagliflozin plus existing oral antidiabetic drugs (OADs), while Group B (n = 18) continued standard care with OADs alone. The study lasted 6 months. Assessments included neuropathic symptoms (MNSI), vibration perception threshold (VPT), corneal confocal microscopy (CNFD, CNBD, CNFL), skin biopsy for intraepidermal nerve fiber density (IENFD), and plasma oxidative stress markers (glutathione peroxidase, malondialdehyde).

## Conclusions

Dapagliflozin was associated with small nerve fibre regeneration and improved oxidative stress in patients with T2DM and DPN.

These findings support the potential disease-modifying role of dapagliflozin in diabetic neuropathy.

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# AMAZING DRUG MOLECULES:

## Drugs Which are Associated with Significant ADRs with Specific Pharmagenetic Biomarkers [Part -1]

Drug molecules associated with Significant ADRs with Specific Pharmagenetic Biomarkers and requires Personalized Therapy in such patients are Tabulated as:

SL No.	Drug	Pharmacogenomic Biomarkers	Clinical Relevance
1	Carbamazepine	HLAB*1501	() Risk of severe skin toxicity
2	Abacavir	HLAB*5701	() Risk of severe skin toxicity
3	Azathioprine & 6-Mercaptopurine	TPMT*3A/*3A(PMs) (Thiopurine S-Methyl transferase)	() Risk of bone marrow aplasia
4	Irinotecan	UGT1A1*28/*28 [Uridine diphosphate glucuronosyl transferase]	() Risk of severe adverse effects (Diarrhea, Bone marrow aplasia)
5	Interferon	IL28B	Variable response in HCV therapy
6	Simvastatin	SLC01B1	() Risk of myopathy
7	Warfarin	VKORC1	(~) Dose requirement
8	Allopurinol	HLA-B*58:01	() Risk of Severe Cutaneous Adverse Reactions [SCARs]
9	Oxcarbazepine	HLA-B*15:02	() Risk of Severe Cutaneous Adverse Reactions [SCARs]
10	Phenytoin	HLA-B*15:02	() Risk of Stevens-Johnson Syndrome [SJS] & Toxic Epidermal Necrolysis [TEN]

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# Extract:



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## What is EXTRACT


Extract are the collections of some important points taken from the discussion in National MD Pharmacology group. NMDP is a group of eminent pharmacologists from all over the country. The head of departments of pharmacology, deans, directors of institutions and people with significant contribution in the field of pharmacology are members of NMDP family. National association of Pharmacology and Therapeutics is promoted by NMDP group.

- **CONSORT2025:** Consolidated Standards of Reporting Trials first published in 1996, then updated in 2001 & 2010. Latest update is published in 2025.
- **Enabling Faculty from Government Hospitals:** Non-teaching government hospitals with 220+ beds can now be designated as teaching institutions. Existing specialists with 10 years of experience can be appointed as Associate Professors, and those with 2 years can be appointed as Assistant Professors—without the mandatory Senior Residency—provided they complete the Basic Course in Biomedical Research (BCBR) within two years.
- **Expanded Recognition of Experience:** Senior Consultants with three years of teaching experience in NBEMS-recognized government medical institutions are eligible for the post of Professor. Diploma holders working as Specialist or Medical Officer in the respective departments of a Government medical institution or Government medical institution running National Board of Examination and Medical Science recognized teaching programme having cumulative experience of six years, shall be eligible for the post of Assistant Professor. They shall have at least two research publications in the concerned specialty during the three years period specified above and must be amongst first 3 three authors.
- **Eligibility for designation as Postgraduate Guide in broad specialties:** NMC Notifies Medical Institutions Regulations, 2025—A faculty member in a medical institution shall be eligible to be designated as a Postgraduate Guide in a broad specialty if such member possesses at least five years of teaching experience in the respective specialty as an Assistant Professor or above.
- **Eligibility for designation as Postgraduate Guide in super specialties:** A faculty member in a medical institution shall be eligible to be designated as a Postgraduate Guide in a super specialty if such member possesses at least three years of teaching experience in the respective super specialty as an Assistant Professor or above.
- **Principal Investigator of M.D. Thesis:** For clinical or interventional studies involving human participants, the PI must be a trained and qualified professional, usually a permanent faculty member. Thesis projects differ from funded research governed by ICMR, where students may be named as Co-Investigators but not PIs internally. In academic research, especially MD thesis, postgraduate students often lead data collection and analysis, but they are typically not designated as Principal Investigators (PI) due to institutional policies and Good Clinical Practice (GCP) requirements. Therefore, the best practice is to credit the student as the investigator and their faculty guide as supervisor, ensuring ethical clarity and institutional compliance.
- **Generic drug prescribing:** Pharmacologists emphasized the importance of prescribing medicines by their generic names, allowing patients to choose between branded, branded generics, or unbranded generics. The real concern lies not in the type of drug but in its quality assurance, especially in India's largely unregulated pharma market. For example, while unbranded generics are cheap, their quality and effectiveness can be questionable. Institutions like AIIMS Delhi and Nagpur are already promoting generic-name prescriptions, supported by initiatives like Jan Aushadhi Kendras. Armed forces have long practiced generic name prescribing. There's also a call for regulatory reforms—like routine batch testing and stricter penalties against substandard drugs—to restore public trust. As one contributor noted, a truly good-quality drug is one that's affordable and manufactured under GMP, regardless of branding.
- **Ecopharmacovigilance Vs Ecopharmacology:** Ecopharmacovigilance studies how medicines, once excreted after use, can enter the environment and potentially harm ecosystems. It aims to track and reduce these effects. Ecopharmacology, meanwhile, looks more broadly at all pharmaceutical and personal care pollutants—no matter how they enter the environment—and how they impact nature and biodiversity.

**National Hands-on Workshop on Clinical Pharmacokinetics :**

Department of Pharmacology, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune, organized a National Hands-on Workshop on Clinical Pharmacokinetics on 23rd and 24th June 2025, under the aegis of National Association of Pharmacology and Therapeutics. Total 51 delegates had registered from various states across India (Maharashtra, Karnataka, Tamil Nadu, Telangana, Odisha, Gujarat and Punjab) of which 47 participants attended the event enthusiastically.

The workshop was inaugurated on 23rd June 2025 at 9.30am by traditional lamp lighting where the expert faculty- Dr.Vipul Chaudhari; Principal- Dr.Karmarkar sir; and Organizing secretary of the workshop- Dr.Priti Dhande formally declared the workshop open. This academic feast was conducted by Dr.Vipul Chaudhari, Professor & Head, Department of Pharmacology, GCS Medical College, Hospital & Research Centre, Ahmedabad, who guided the participants through interactive sessions and practical applications in clinical pharmacokinetics. The workshop was highly appreciated by all participants who were engaged on both the days of workshop solving complex problems on pharmacokinetics with same enthusiasm.



The poster features a blue background with a faint image of pills. At the top left is the Bharati Vidyapeeth logo, and at the top right is the National Association of Pharmacology and Therapeutics logo. The title 'National Workshop on CLINICAL PHARMACOKINETICS' is in a dark blue box. Below the title are four hexagonal images: a pharmacokinetic graph, a person in a lab coat, a person using a pipette, and various pills. The dates '23<sup>rd</sup> & 24<sup>th</sup> June, 2025' are in the center. A starburst graphic states 'only 50 seats for registered participants'. The organizing department is listed as 'Department of Pharmacology, Bharati Vidyapeeth (DU) Medical College, Pune'. It is organized under the aegis of the 'National Association of Pharmacology & Therapeutics'. The expert faculty is 'Dr. Vipul Chaudhari, Professor & Head, Department of Pharmacology, GCS Medical College, Hospital & Research Centre, Ahmedabad'. A circular portrait of Dr. Vipul Chaudhari is at the bottom left.

**National Workshop on  
CLINICAL  
PHARMACOKINETICS**

**23<sup>rd</sup> & 24<sup>th</sup> June, 2025**

**only 50  
seats  
for registered  
participants**

**Organized by  
Department of Pharmacology  
Bharati Vidyapeeth (DU) Medical College, Pune**

**Under the aegis of  
National Association of Pharmacology & Therapeutics**

**Expert Faculty  
Dr. Vipul Chaudhari  
Professor & Head  
Department of Pharmacology  
GCS Medical College, Hospital  
& Research Centre, Ahmedabad**



**ORGANIZING SECRETARY**  
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### Workshop Schedule

#### Day 1

- 09.00 AM- 09.30 AM - Registration & Breakfast
- 09.30 AM - 10.00 AM - Inauguration of Workshop
- 10.00 AM - 11.30 AM -
  - Introduction to Pharmacokinetics
  - Compartmental Models
  - Concept and Calculation of Bioavailability (F)
  - Concept and Calculation of Drug Distribution (aVD)
- 11.30 AM - 11.45 AM - Tea Break
- 11.45 AM - 01.15 PM -
  - Mathematical concept of log/ln
  - Use of Semilog Paper
  - Concept of first and zero order kinetics and its calculation on semilog paper
- 01.15 PM - 02.00 PM - Lunch Break

#### Day 2

- 09.00 AM- 09.30 AM - Recap of Day 1 Workshop
- 09.30AM - 11.00 AM -
  - Elimination Rate Constant ( $k_{el}$ )
  - Half-life and its calculation.
  - AUC Measurements by 3 methods
  - Concept of Drug Clearance (CL)
- 11.00 AM - 11.15 AM- Tea Break
- 11.15 AM - 12.45 PM -
  - Loading & Maintenance Dose
  - Concept of Steady state concentration ( $C_{ss}$ ) & PK parameters affecting  $C_{ss}$
  - Question & Answer Session
- 12.45 PM - 01.15 PM - Group Photograph & Certificate Distribution
- 01.15 PM - 02.00 PM - Lunch Break





# NATIONAL ASSOCIATION OF PHARMACOLOGY AND THERAPEUTICS

Promoting Pharmacology and Therapeutics for a better tomorrow

## About the organization

A national organization of medical doctors specialized in pharmacology /clinical pharmacology and therapeutics. Envisaged to provide strong leadership to promote pharmacology and therapeutics for a better tomorrow. The association is fostered by NMDP (National MD Pharmacology), a prestigious group of eminent pharmacologists.

## Aims and objectives

Empowering medical doctors specialized in Pharmacology/Clinical Pharmacology and Therapeutics.  
Promoting academic and clinical research in Pharmacology/Clinical Pharmacology and Therapeutics.  
Enhancing the standard of teaching/training in Pharmacology/Clinical Pharmacology and Therapeutics  
Promoting Pharmacology/Clinical Pharmacology and Therapeutics for the benefit of patients and society.



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Participate in general body meetings (GBM) to speak and to vote.

Participate in conferences/seminars/workshops/symposiums/training sessions at subscribed charges.

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## NATIONAL ASSOCIATION OF PHARMACOLOGY AND THERAPEUTICS

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# R<sub>x</sub> FACTOR

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## NATIONAL ASSOCIATION OF PHARMACOLOGY AND THERAPEUTICS

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