SLACPT NEWS

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the Sri Lanka Association of
Clinical Pharmacology and Therapeutics

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SLACPT THEME 2025-2026

Personalized Medicine : Shaping the Future of Prescribing

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President's Message

Dear Colleagues and Friends,

As the 1st year of the present Council's tenure draws to a close, it is time to reflect on what has been and look forward to what will be.

I am happy to report that we have been able to successfully conclude most of the scheduled activities of the SLACPT's for 2025. We have had to postpone the training session on Medical Illustrations and the webinar planned with Sri Lanka College of Internal Medicine due to unforeseen circumstances. These will be rescheduled, and the new dates will be informed to you.

We are moving ahead with the preparations for the Biennial Scientific Sessions. The sessions will be held on 6th and 7th of August 2026. Please keep the dates free, we will let you know the details of the programme and the venue once finalised. The call for abstracts is shared with you in this issue of the newsletter, and I invite you to submit your abstracts to enrich the deliberations of the sessions.

To all of you,

Compliments of the Season and Best wishes for 2026! May the New Year bring you joy, happiness and fulfilment in abundance.

Professor Chandanie Wanigatunge
President, SLACPT

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Cover Story

The journey of drug discovery and development across the 20th and 21st centuries reflects one of the most remarkable transformations in modern science. From early pharmacopoeias grounded in botanical knowledge and empirical practice, medicine evolved through the rise of the pharmaceutical industry, laboratory science, and industrial-scale drug production.

Breakthroughs in chemistry, microbiology, and molecular biology laid the foundations for rational drug design and evidence-based therapeutics.

Equally transformative was the establishment of robust scientific and ethical frameworks governing drug development. The emergence of controlled clinical trials, regulatory oversight, and Good Clinical Practice ensured that innovation was guided by safety, efficacy, and respect for human dignity.

Today, advances in genomics, biotechnology, and precision medicine continue this evolution, bridging tradition with technology.

SLACPT 75th Council Meeting - 13th of October 2025

The Seventy-Fifth Council Meeting of the Sri Lanka Association of Clinical Pharmacology and Therapeutics was held on the 13th of October 2025 at the Department of Pharmacology, Faculty of Medical Sciences, University of Sri Jayewardenepura.

Before the commencement of the 75th Council meeting of SLACPT, the President presented the trophy to the winning team from the Faculty of Medicine, University of Colombo, who won the SLACPT Inter-Medical Faculty Pharmacology Quiz 2025.

Winners of the Pharmacology Quiz

University of Colombo

Visal Perera
Dinal De Silva
S. Tharsikan
Sachini Wijewardena
Hirusha Fernando

A Journey of the Discovery and Development of Drugs: From Empiricism to Ethics

Sahan Mendis
Department of Pharmacology, Faculty of Medicine, University of Ruhuna

The 20th century stands as a transformative era in the history of medicine, marking the evolution of drug discovery and development from empirical practice to a scientifically rigorous and ethically governed enterprise. This period witnessed the birth of the modern pharmaceutical industry, the establishment of systematic drug evaluation, and a profound ethical reckoning that reshaped biomedical research globally.

Establishing a Scientific Basis for Drug Trials

Parallel to industrial growth was the maturation of scientific methods used to evaluate medicines. Early clinical use often relied on anecdotal experience and uncontrolled observations. However, growing recognition of variability, bias, and harm led to the development of structured clinical experimentation.

The introduction of controlled trials, statistical methods, dose-response analysis, and eventually randomised controlled trials (RCTs) transformed drug development into a disciplined scientific process. Regulatory milestones—such as the establishment of the U.S. Food and Drug Administration (FDA) and the 1962 Kefauver-Harris Amendments—mandated proof of both safety and efficacy before approval. This period laid the foundations of modern clinical pharmacology and evidence-based medicine.

The Rise of the Pharmaceutical Industry

At the dawn of the 20th century, drug therapy was largely based on natural products, serendipitous observations, and limited experimental validation. This landscape changed dramatically with advances in chemistry, microbiology, and industrial manufacturing. Landmark discoveries such as aspirin, insulin, sulfonamides, and penicillin demonstrated that diseases could be systematically targeted with specific chemical agents.

These successes catalysed the emergence of the pharmaceutical industry, particularly in Europe and the United States. Companies evolved from small chemical manufacturers into research-driven organisations with dedicated laboratories, multidisciplinary teams, and large-scale production capabilities. By mid-century, pharmaceutical enterprises had become central players in healthcare, innovation, and global medicine.

From Atrocity to Accountability: The Ethical Awakening

The most sobering transformation of 20th-century research arose from ethical failures during the Nazi era, where inhumane experiments were conducted without consent, scientific justification, or regard for human dignity. These atrocities exposed the dangers of unregulated research and forced the global scientific community to confront the moral dimensions of experimentation.

The Nuremberg Trials culminated in the Nuremberg Code (1947), establishing voluntary informed consent as an absolute requirement. This was followed by the Declaration of Helsinki, the Belmont Report, and the evolution of institutional ethics review mechanisms. These frameworks redefined research as a moral contract between investigators and participants.

The Era of Good Clinical Practice

By the late 20th century, ethical principles were codified into operational standards known as Good Clinical Practice (GCP). GCP integrated scientific rigor with ethical responsibility, ensuring participant safety, data integrity, transparency, and accountability. Ethics committees, informed consent processes, pharmacovigilance, and regulatory oversight became integral to drug development.

This shift marked a decisive transition from viewing human subjects as experimental means to recognising them as protected partners in research. Ethical governance became not a barrier, but a cornerstone of credible and socially responsible science.

Conclusion

The evolution of drug discovery and development in the 20th century reflects a journey from chance discovery to controlled science, and from moral failure to ethical accountability. The modern pharmaceutical ecosystem, anchored in industry, evidence, and ethics, is a legacy shaped by both remarkable achievements and hard-learned lessons. As we move into an era of precision medicine and pharmacogenomics, these historical foundations remain essential to ensuring that innovation continues to serve humanity with integrity and trust.

Reference

Drews, J. (2000). Drug discovery: A historical perspective. Science, 287(5460), 1960–1964.

Capacity Building Workshop Series

The SLACPT Capacity Building Workshop aims to enhance the knowledge and practice of clinical pharmacologists regarding their professional responsibilities. Second session of this series was held as a hybrid session on the 13th of October 2025 at the Department of Pharmacology, Faculty of Medical Sciences, University of Sri Jayewardenepura.

Two insightful and highly informative sessions were delivered on:

"Challenges in the Classification and Registration of Borderline Products"
by Professor Menik Hettihewa

"Teaching and Assessment on the Safe Use of Medicines"
by Professor Priyadarshani Galappatthy

The Pharmacology of the Season: When Festivities Meet Medicines

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The period from December to January is a season of celebration, indulgence, and altered routines. It is also a period when pharmacology quietly plays a central role. Changes in diet, alcohol intake, sleep patterns, and medication adherence can significantly influence drug pharmacokinetics and pharmacodynamics.

Alcohol consumption often increases during the festive season, heightening the risk of hepatotoxicity, particularly in individuals using paracetamol. Paracetamol is primarily metabolised in the liver by glucuronidation and sulfation, with a small proportion converted via the cytochrome P450 system (mainly CYP2E1) to the toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI), which is normally detoxified by hepatic glutathione. Acute binge drinking rapidly reduces hepatic glutathione stores, impairing NAPQI detoxification and increasing the risk of hepatotoxicity, even at therapeutic doses. Meanwhile, chronic alcohol consumption induces hepatic CYP2E1 activity, increasing the proportion of paracetamol metabolised to the toxic intermediate N-acetyl-p-benzoquinone imine (NAPQI).

In individuals with long-standing alcohol use, particularly those with malnutrition or underlying liver disease, this enhanced NAPQI production, combined with reduced glutathione reserves, markedly increases susceptibility to paracetamol-induced hepatotoxicity. Alcohol also potentiates the sedative effects of benzodiazepines, opioids, and first-generation antihistamines, increasing the risk of respiratory depression, impaired cognition, and falls. Additionally, alcohol can enhance the hypotensive effects of nitrates, alpha-blockers, and antihypertensives, predisposing to syncope.

NSAID use rises during holidays for musculoskeletal aches and headaches. When combined with dehydration, reduced oral intake, ACE inhibitors or ARBs, and diuretics, NSAIDs can precipitate acute kidney injury, particularly in older adults. NSAIDs also increase gastrointestinal bleeding risk, especially in those already on aspirin, anticoagulants (warfarin, DOACs), or corticosteroids.

Polypharmacy becomes particularly hazardous during this season, with increased use of over-the-counter remedies. Cold and flu preparations may contain sympathomimetics such as pseudoephedrine or phenylephrine, which can exacerbate hypertension, arrhythmias, and ischemic heart disease, and interact adversely with beta-blockers, MAO inhibitors, and tricyclic antidepressants. Many combination products also contain paracetamol, increasing the risk of unintentional overdose when patients self-medicate alongside prescribed analgesics.

Festive foods introduce additional pharmacological considerations. Grapefruit juice (*Jambola)* inhibits CYP3A4, increasing serum concentrations of drugs such as statins (simvastatin, atorvastatin), calcium channel blockers, amiodarone, and certain benzodiazepines, raising the risk of myopathy, hypotension, and toxicity. Large, vitamin K–rich meals may antagonise warfarin, while alcohol and cranberry products can unpredictably alter INR control.

Even the neuropharmacology of the season is noteworthy. Dopaminergic reward pathways are stimulated by festive foods and social interactions, reinforcing hedonic eating behaviours.

Altered melatonin secretion due to late nights and artificial lighting disrupts circadian rhythms, often leading to inappropriate or excessive use of hypnotics and sedatives, which may accumulate in older adults. In vulnerable individuals, reduced sunlight exposure may exacerbate seasonal affective symptoms, influencing antidepressant adherence and, in some cases, prompting unsupervised dose adjustments.

This festive season offers a timely reminder that medicines do not exist in isolation. Understanding how festive behaviours modify drug effects allows us to anticipate complications, counsel patients effectively, and ensure safer prescribing during this unique time of year.

Adverse Drug Reactions and Pharmacovigilance for the Prescriber

Chandanie Wanigatunge
Department of Pharmacology, Faculty of Medical Sciences, University of Sri Jayewardenepura

Adverse drug reactions (ADRs) can occur with any medicine. An ADR is defined as any response to a drug that is noxious and unintended, and that occurs at doses normally used in humans for the prophylaxis, diagnosis, or treatment of disease, or for the modification of physiological function. These reactions may be known, either common or rare, or previously unknown and reported for the first time.

A suspected adverse event (SAE) is an untoward medical occurrence that may appear during or after treatment with a drug and is suspected to be caused by the drug. If the suspected drug is identified as a likely cause of the SAE following expert review, the event is classified as an ADR.

Why do ADRs occur?

1. Medicines may act at sites or on receptors other than those intended by the prescriber. The effects arising from such actions may be harmful and lead to ADRs.

2. Comorbid conditions can affect the metabolism and elimination of medicines, resulting in drug accumulation beyond the therapeutic range and increasing the risk of ADRs.

3. Idiosyncratic reactions may cause allergies and anaphylaxis. The risk of such reactions may be known or unknown.

4. Quality-related issues, including impurities that should not be present in the product and improper storage conditions, may also result in ADRs.

What is pharmacovigilance?

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine- or vaccine-related problem.

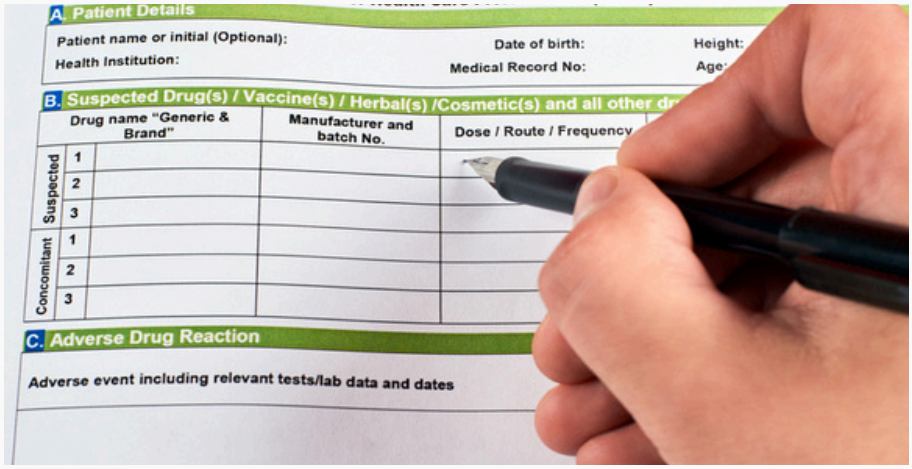
Why do we need pharmacovigilance?

Medicines undergo rigorous testing during development to demonstrate their effectiveness and to identify potential adverse effects. However, clinical trials are limited by design and often involve selected populations. Some adverse effects may only become evident after medicines are released to the market and used by a heterogeneous population, including individuals with comorbidities.

Identifying adverse effects helps ensure that medicine use is both safe and effective for individual patients.

Why should ADRs be reported?

Reports from healthcare professionals are a vital source of information that enables the regulator, in Sri Lanka, the National Medicines Regulatory Authority (NMRA), to detect, investigate, and take appropriate action to improve the safety of medicines and vaccines.

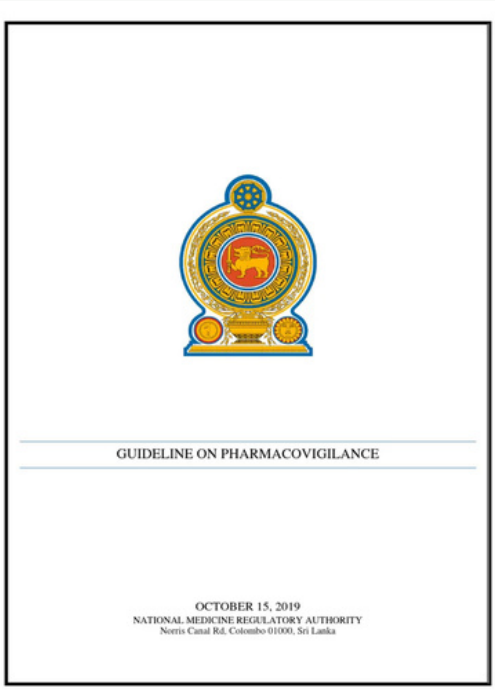


What should prescribers do?

Adverse events should be reported even when causality is uncertain, as individual reports may contribute to the identification of new or rare safety signals.

Suspected adverse effects should be reported to the relevant authorities to support pharmacovigilance activities. In Sri Lanka, the focal point for pharmacovigilance is the Pharmacovigilance Unit of the NMRA. (https://www.nmra.gov.lk/pages/pharmacovigilance)

Reporting adverse events to the NMRA is mandatory for sponsors (pharmaceutical companies) who are required to carry out post-marketing surveillance. It is strongly encouraged but is voluntary for healthcare professionals and consumers.



However, there are many barriers to adverse event reporting by healthcare professionals, including lack of time, the perception that reporting is not important, and insufficient knowledge and training on what events to report, and how to report them.

Table 1: Misconceptions/questions about ADR reporting

Misconceptions/ questions	Truth/answers
Adverse events should only be reported if serious, recurrent or proven.	Any adverse event can be reported, even if there is only a suspicion that it was caused by a medicine or vaccine. Confirmation can only be done after a root cause analysis.
Adverse event reporting is limited to prescribed medicines and vaccines.	Adverse events for any medicine or vaccine can be reported, including over-the-counter medicines and borderline products.
Only the prescriber of the suspected medicine or vaccine can report.	Anyone can report an adverse event, including nurses, pharmacists or any other healthcare professional.
A single adverse event is not worth reporting.	Anyone can report an adverse event, including nurses, pharmacists or any other healthcare professional.
Do not know how and where to make the report.	Adverse events can be reported online through the NMRA's adverse event reporting website, via a Google form. If a paper copy is filled, ensure that the correct form is filled – for anaphylaxis (pink form) and all other reactions for medicines/borderline products (white form). The completed forms should be emailed to pharmcovigilance@nmra.gov.lk All forms are available from: https://www.nmra.gov.lk/pages/pharmacovigilance

Modified from (2)

The information that should be submitted is detailed in the ADR reporting form available from https://www.nmra.gov.lk/pages/pharmacovigilance.

This information should include:
1. details of the patient
2. details of the suspected medicine
3. details of adverse reaction
4. details of other medicines taken at the same time
5. details of the person reporting the details

ADRs should be reported as soon as suspected, even if all the details requested in the form are not available. The NMRA will contact the person submitting the details for further information if needed.
If quality issues are suspected as the cause of ADR, samples of the product should be submitted to NMRA.

Causality assessment

Causality assessment is conducted to determine the likelihood that a suspected drug caused an ADR. The likelihood is classified as "certain", "probable", "possible", "unlikely", or "unassessable/unclassifiable" based on the factors given in Table 2. If relevant data is not available, the reaction is considered "unclassifiable". These categories are defined by the World Health Organization and the Uppsala Monitoring Centre (3).

Table 2 Classification of ADRs based on the causality assessment

Criterion	Certain	Probable/ likely	Possible	Unlikely (but NOT impossible)	Unassessable/ unclassifiable
Time sequence is reasonable	Yes	Yes	Yes	No	Information not available or not possible to verify accuracy
Events are known to be of the drug	Yes	Yes	Yes	Unlikely but possible	
Events are explained by comorbidities	No	No	Yes	Yes	
Events were reversed after stopping the drug	Yes	Yes	Uncertain (Information lacking or not conclusive)	No information available	
Rechallenge done and the event recurred	Yes	Not done	Not done	Not done	

Note that it is unethical to rechallenge with the suspected medicine unless it is absolutely essential and no other option is available. Therefore, most of the ADRs would be classified as “probable” or “possible” in most instances.

Summary

Adverse drug reactions (ADRs) can occur with any medicine and may be known, rare, or previously unidentified. Many ADRs only become apparent after medicines are widely used, as clinical trials involve limited and selected populations. Pharmacovigilance is essential for detecting, assessing, and preventing medicine- and vaccine-related harms throughout their lifecycle. Reporting suspected adverse events, even when causality is uncertain, contributes to early signal detection and improved patient safety. Active participation by prescribers and other healthcare professionals strengthens regulatory decision-making and promotes safer and more effective use of medicines.

References

1.https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance

2. Greenbaum D, Cheung S, Turner C, Mackinnon F, Larter C. Pharmacovigilance in Australia: how do adverse event reports from clinicians contribute to medicine and vaccine safety?. Aust Prescr 2024;47:18691. https://doi.org/10.18773/austprescr.2024.056

3. https://www.who.int/docs/default-source/medicines/pharmacovigilance/whocausality-assessment.pdf

Drug Information Summary

Semaglutide

Semaglutide is a long-acting, once-weekly, subcutaneous glucagon-like peptide-1 (GLP-1) receptor agonist that improves glycaemic control and promotes weight reduction in adults with type 2 diabetes mellitus (T2DM). It exerts glucose-dependent effects on insulin and glucagon secretion, delays gastric emptying, and reduces appetite and energy intake. Semaglutide has demonstrated robust benefits on glycaemic control, body weight, cardiovascular outcomes, and kidney disease progression, distinguishing it as a key disease-modifying therapy in modern diabetes management

Mechanism of Action

Semaglutide is a GLP-1 analogue (94% homology to native human GLP-1) that selectively binds to and activates the GLP-1 receptor. Its actions include:
Glucose-dependent stimulation of insulin secretion
Suppression of inappropriate glucagon secretion
Delay of early post-prandial gastric emptying
Central appetite suppression with reduced energy intake and preference for high-fat foods

It lowers blood glucose without impairing counter-regulatory glucagon responses during hypoglycaemia and promotes sustained weight and fat mass reduction. GLP-1 receptors expressed in cardiovascular and renal tissues contribute to its pleiotropic cardiometabolic benefits

Pharmacokinetic Properties

Absorption

Route: Subcutaneous
Time to peak concentration: 1–3 days post-dose
Steady state: Achieved after 4–5 weeks of once-weekly dosing

Distribution

Extensive albumin binding, contributing to prolonged action
Large apparent volume of distribution

Metabolism and Elimination

Protected from degradation by DPP-4
Reduced renal clearance due to albumin binding
Half-life: ~1 week, enabling once-weekly administration

Special Populations

Renal impairment: No dose adjustment required (limited data in end-stage kidney disease)
Hepatic impairment: No dose adjustment required; limited experience in severe impairment
Paediatrics: Safety and efficacy not established (<18 years)

Therapeutic Indications

Adults

Treatment of type 2 diabetes mellitus inadequately controlled with diet and exercise:
As monotherapy when metformin is inappropriate
As add-on therapy to other glucose-lowering agents, including insulin
Semaglutide has demonstrated reductions in:
Major adverse cardiovascular events (MACE)
Progression of chronic kidney disease
Body weight and systolic blood pressure

Posology and Method of Administration

Adults

Starting dose: 0.25 mg once weekly (non-maintenance dose)
After 4 weeks: Increase to 0.5 mg once weekly
Further titration:
1 mg once weekly after ≥4 weeks
2 mg once weekly after ≥4 weeks if additional glycaemic control required
Maximum recommended dose: 2 mg once weekly

Concomitant Therapy

Metformin, thiazolidinediones, SGLT2 inhibitors: continue unchanged
Sulfonylurea or insulin: consider dose reduction to reduce hypoglycaemia risk

Missed Dose

Administer within 5 days of the missed dose
If >5 days, skip and resume on the scheduled day

Administration

Subcutaneous injection into abdomen, thigh, or upper arm
Can be administered with or without meals
Not for intravenous or intramuscular use

Contraindications

Hypersensitivity to semaglutide or excipients

Special Warnings and Precautions

Not indicated for type 1 diabetes or diabetic ketoacidosis
Gastrointestinal adverse effects (nausea, vomiting, diarrhoea) may cause dehydration and worsen renal function
Acute pancreatitis: discontinue if suspected or confirmed
Hypoglycaemia risk increased with sulfonylurea or insulin
Diabetic retinopathy: risk of complications in insulin-treated patients with rapid glycaemic improvement
Non-arteritic anterior ischaemic optic neuropathy (NAION): rare but reported; discontinue if confirmed

General anaesthesia/deep sedation: risk of aspiration due to delayed gastric emptying
Not recommended in NYHA class IV heart failure

Drug Interactions
Delayed gastric emptying may affect absorption of oral medicines requiring rapid uptake
No clinically relevant interactions with:
Metformin
Atorvastatin
Digoxin
Oral contraceptives
Warfarin/coumarins: INR monitoring recommended on initiation
Paracetamol exposure unaffected overall

Fertility, Pregnancy and Lactation
Pregnancy: Not recommended; discontinue at least 2 months before planned pregnancy
Breastfeeding: Not recommended (excreted in animal milk)
Fertility: No adverse effects in males; minor effects on oestrous cycle in animals

Adverse Effects
Common Adverse Effects
Gastrointestinal: Nausea, diarrhoea, vomiting, abdominal pain, constipation, dyspepsia
General: Fatigue, injection-site reactions
Metabolic: Decreased appetite, weight loss
Uncommon to Rare
Acute pancreatitis
Cholelithiasis
Diabetic retinopathy complications
Increased heart rate
Hypersensitivity reactions, including angioedema
Most gastrointestinal effects are mild-to-moderate, dose-dependent, and occur early in treatment

Pharmacodynamic Effects
Reduces fasting and post-prandial glucose concentrations
Improves β-cell function and insulin secretory capacity
Lowers fasting and post-prandial glucagon
Produces clinically meaningful and sustained weight loss
Reduces systolic blood pressure, triglycerides, and VLDL cholesterol
Demonstrated 26% reduction in major adverse cardiovascular events and significant slowing of kidney disease progression in high-risk populations

Semaglutide Overdose: Key Points

No specific antidote

Most common effect: nausea

Management is supportive, with prolonged observation due to long half-life (~1 week)

All reported overdose cases recovered without complications

Source:

Summary of Product Characteristics of Semaglutide, European Medicines Agency (EMA)

Detailed information of this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu/.

Drug Information Summary

Bempedoic Acid

Bempedoic acid is an oral, once-daily lipid-lowering agent that reduces low-density lipoprotein cholesterol (LDL-C) by inhibiting hepatic cholesterol synthesis upstream of HMG-CoA reductase. It is indicated for adults with primary hypercholesterolaemia or mixed dyslipidaemia, including those who are statin-intolerant or unable to achieve LDL-C targets despite maximally tolerated statin therapy. By selectively targeting liver-specific pathways, bempedoic acid provides effective LDL-C reduction with a low risk of skeletal muscle–related adverse effects and has demonstrated cardiovascular risk reduction in high-risk populations.

Mechanism of Action

Bempedoic acid is an adenosine triphosphate citrate lyase (ACL) inhibitor. ACL is an enzyme located upstream of HMG-CoA reductase in the hepatic cholesterol biosynthesis pathway.

Bempedoic acid is a prodrug that requires activation by very-long-chain acyl-CoA synthetase-1 (ACSVL1), an enzyme expressed primarily in the liver but not in skeletal muscle. After intracellular activation to its CoA-conjugated form, inhibition of ACL leads to:

Reduced hepatic cholesterol synthesis
Up-regulation of LDL receptors
Increased clearance of LDL-C from the circulation
This liver-selective activation explains the low incidence of myopathy compared with statins

Pharmacokinetic Properties

Absorption

Route: Oral
Time to peak concentration (Tmax): ~3.5 hours
Steady state: Achieved after ~7 days
Food does not affect overall bioavailability, though it slows absorption

Distribution

Volume of distribution: ~18 L
Plasma protein binding: >99%
Does not partition into red blood cells

Metabolism and Elimination

Not metabolised by cytochrome P450 enzymes
Primarily metabolised to an acyl-glucuronide conjugate
Minor reversible conversion to an active metabolite (ESP15228)
Renal excretion of unchanged drug: <2%
Half-life: ~19 hours

Special Populations
Renal impairment: Increased exposure in severe impairment and ESRD; no dose adjustment recommended, but additional monitoring advised
Hepatic impairment: No adjustment required in Child-Pugh A or B; not studied in Child-Pugh C
Paediatrics: Safety and efficacy not established (<18 years)

Therapeutic Indications
Adults
Primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- In combination with a statin (± other lipid-lowering therapies) when LDL-C targets are not achieved.
- Alone or in combination with other lipid-lowering therapies in statin-intolerant patients or when statins are contraindicated.
- Cardiovascular disease risk reduction in adults with established or high-risk atherosclerotic cardiovascular disease, by lowering LDL-C levels.

Posology and Method of Administration
Adults
Recommended dose: 180 mg once daily

Concomitant Therapy
May be used with statins, ezetimibe, or other lipid-lowering therapies
Simvastatin:
Limit dose to ≤20 mg daily
Up to 40 mg daily only in selected high-risk patients when benefits outweigh risks

Special Populations
Elderly: No dose adjustment required
Renal impairment: No dose adjustment; monitor in severe impairment
Hepatic impairment: No adjustment in mild/moderate impairment

Administration
Oral administration with or without food
Tablet should be swallowed whole

Contraindications
Hypersensitivity to bempedoic acid or excipients
Pregnancy
Breast-feeding
Concomitant use with simvastatin doses >40 mg daily

Special Warnings and Precautions
Myopathy risk with statins: Increased statin exposure; monitor for muscle symptoms and creatine kinase elevation
Hyperuricaemia and gout: Serum uric acid may increase; discontinue if symptomatic gout occurs
Hepatic enzyme elevations: Perform liver function tests at initiation and discontinue if persistent >3× ULN
Renal impairment: Monitor renal parameters, especially in severe impairment or ESRD
Women of child-bearing potential: Effective contraception required

Drug Interactions
Statins: Increased exposure (particularly simvastatin); dose restrictions apply
OATP1B1/1B3 substrates: May increase plasma concentrations
Ezetimibe: Mild increase in exposure; not clinically relevant
Probenecid: Increases exposure; no dose adjustment required
No clinically meaningful interactions with:
Metformin

Fertility, Pregnancy and Lactation
Pregnancy: Contraindicated; discontinue prior to conception
Breast-feeding: Contraindicated
Fertility: No expected effects based on animal studies

Adverse Effects
Common Adverse Effects
Metabolism: Hyperuricaemia, gout
Blood: Anaemia
Musculoskeletal: Pain in extremities
Hepatobiliary: AST elevation
Renal: Decreased glomerular filtration rate

Uncommon Adverse Effects
Decreased haemoglobin
ALT elevation
Increased creatinine and blood urea
Weight reduction (mainly in obese patients)
Most laboratory abnormalities occur early, are reversible, and return to baseline after discontinuation

Pharmacodynamic Effects

Reduces LDL-C, non-HDL-C, apolipoprotein B, and total cholesterol
Lowers C-reactive protein, reflecting anti-inflammatory effects
Modest reduction in HbA1c (~0.2%) observed in patients with diabetes
Does not prolong QT interval
In the CLEAR Outcomes trial, bempedoic acid reduced:
MACE-4 by 13%
MACE-3 by 15%, driven by reductions in non-fatal myocardial infarction and coronary revascularisation

Bempedoic Acid Overdose: Key Points

No specific antidote
Doses up to 240 mg/day showed no dose-limiting toxicity
Management is symptomatic and supportive

Source:

Summary of Product Characteristics of Bempedoic Acid, European Medicines Agency (EMA)
Detailed information of this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu/.

Emerging Pharmacotherapies in Obesity

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[2]Department of Clinical Medicine, Faculty of Medicine, University of Colombo

In the previous newsletter, we explored the rapidly evolving landscape of novel pharmacological therapies for obesity, with a particular focus on glucagon-like peptide-1 (GLP-1) analogues, dual GLP-1/GIP receptor agonists, triple agonists such as retatrutide targeting GLP-1, GIP, and glucagon receptors, and emerging tetra-agonist therapies. . While GLP-1–based therapies have transformed the pharmacological landscape of obesity, a new wave of agents targeting central appetite regulation, adipose tissue biology, and metabolic signalling is rapidly emerging. These therapies aim not only to reduce body weight, but also to preserve lean mass, improve cardiometabolic health, and address obesity-related conditions such as metabolic dysfunction–associated steatohepatitis (MASH).

Triple Monoamine Reuptake Inhibitors

Triple monoamine reuptake inhibitors act centrally by inhibiting the reuptake of noradrenaline, serotonin, and dopamine, thereby suppressing appetite and increasing energy expenditure.

Sibutramine, one of the earliest agents in this class, demonstrated significant weight loss through appetite suppression and enhanced thermogenesis. However, post-marketing studies revealed increased heart rate and blood pressure, leading to higher cardiovascular risk. Consequently, sibutramine was withdrawn from the market in several countries due to safety concerns (1-3).

Tesofensine, initially investigated for Alzheimer's and Parkinson's disease, was noted to cause marked appetite suppression and weight loss during early trials (4). Subsequent studies in obesity have shown promising weight-loss efficacy, although long-term cardiovascular safety remains under close evaluation.

Dual SGLT1/2 Inhibition: Sotagliflozin

Sotagliflozin is a dual inhibitor of sodium–glucose cotransporters SGLT1 and SGLT2, reducing both intestinal glucose absorption and renal glucose reabsorption.

In the phase 3 inTandem3 randomized controlled trial, sotagliflozin led to a mean weight reduction of 2.98 kg over 24 weeks compared with placebo (5). Beyond weight loss, its glycaemic benefits highlight the potential role of SGLT1/2 inhibition in patients with obesity and diabetes.

ActRIIB Inhibition: Bimagrumab

Bimagrumab (BYM338) is a fully human monoclonal antibody targeting type II activin receptors (ActRII). By blocking ligands such as myostatin and activins, which negatively regulate skeletal muscle growth, bimagrumab promotes muscle hypertrophy and prevents muscle wasting (6,7).

Inhibition of ActRIIB also stimulates brown adipogenesis and thermogenesis through enhanced mitochondrial function (8). In a recent phase 2 randomized clinical trial, 48 weeks of bimagrumab therapy significantly increased lean mass while reducing total body fat and improving glycaemic control in patients with obesity (9). This unique profile positions bimagrumab as a potential therapy for obesity with sarcopenic risk.

Novel Incretin-Based and Multimodal Agents

Several next-generation agents combine incretin pathways to enhance weight loss while targeting metabolic comorbidities:

· MariTide (maridebart caflaglutide) is an engineered molecule combining a GIP receptor antagonist with a GLP-1 receptor agonist. Early studies demonstrate an acceptable safety profile and pronounced dose-dependent weight loss (10).

· Mazdutide (IBI362 / LY3305677) and Survodutide are dual GLP-1 and glucagon receptor agonists. Once-weekly subcutaneous mazdutide has shown good tolerability with meaningful weight loss over 12 weeks (11). Survodutide has additionally demonstrated improvement in MASH without worsening fibrosis in phase 2 trials (12).

· Efinopegdutide, another GLP-1–glucagon co-agonist, showed a greater reduction in liver fat content at a 10 mg weekly dose compared with semaglutide 1 mg weekly, highlighting its potential role in obesity-associated liver disease (13).

· The novel oral formulation of semaglutide has also expanded therapeutic options. In the PIONEER PLUS trial, oral semaglutide was shown to be safe and effective in reducing body weight and HbA1c in adults with diabetes (14).

Adipose Tissue–Targeted Therapies

Adipose tissue is increasingly recognized as a dynamic and therapeutically modifiable organ. It exists primarily as white adipose tissue (WAT), responsible for energy storage, and brown adipose tissue (BAT), which is metabolically active and capable of heat generation via non-shivering thermogenesis (15).

BAT activation is mediated through β3-adrenergic receptors, making these receptors attractive therapeutic targets (16). Mirabegron, a β3-adrenergic agonist, has shown mixed results regarding weight loss but has consistently demonstrated improvements in glucose homeostasis.

WAT has also become a focus of nanotherapeutic strategies, including:

Inhibition of angiogenesis to limit adipose tissue expansion (17)

Browning of WAT through enhanced mitochondrial biogenesis (18)

Photothermal lipolysis using targeted nanoparticles (19)

Agents such as dibenzazepine and rosiglitazone (a PPAR-γ activator) are being investigated using targeted nanoparticle delivery systems to confine browning effects to adipose tissue. Pre-clinical studies involving dibenzazepine-loaded nanoparticles (20) and rosiglitazone-loaded nanoparticles (21) have demonstrated promising metabolic effects while potentially minimizing systemic adverse outcomes.

Looking Forward

The future of obesity pharmacotherapy is rapidly evolving beyond simple appetite suppression. Emerging agents aim to reset energy balance, preserve lean mass, improve metabolic health, and treat obesity-related organ dysfunction, including MASH.

In the next issue, we will explore emerging and established pharmacological therapies for non-alcoholic fatty liver disease

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Wall of Fame

Professor Chamila Mettananda
Professor in Pharmacology, Faculty of Medicine, University of Kelaniya, delivered the prestigious **Ceylon College of Physicians Oration** at the Annual Academic Sessions of Ceylon College of Physicians 2025 titled **"From Data to Diagnosis: Revolutionizing Cardiovascular Risk Assessment in Sri Lanka with AI"** on the 10th of September 2025.

Professor Priyanga Ranasinghe
Professor in Pharmacology, Faculty of Medicine, University of Colombo, delivered the prestigious **Professor P.B. Fernando Memorial Oration** at the Annual Academic Sessions of Ceylon College of Physicians 2025 titled **"Translating Traditional Knowledge into Evidence-based Herbal Medicine: The Case of Ceylon Cinnamon"** on the 11th of September 2025.

SLACPT upcoming events

SLACPT/SLCIM Joint CME Webinar – February 2026

Next SLACPT joint CME webinar will be conducted in collaboration with Sri Lanka College of Internal Medicine in February 2026 on Clinical Toxicology

Topics to be discussed:

- Approach to managing medication overdose
- Psychoactive drug overdose – Opioids/amphetamines
- Deliberate self harm and psychiatric drug overdose
- Approach to management of paracetamol overdose

"ClinPharm" - SLACPT Scientific Sessions 2026

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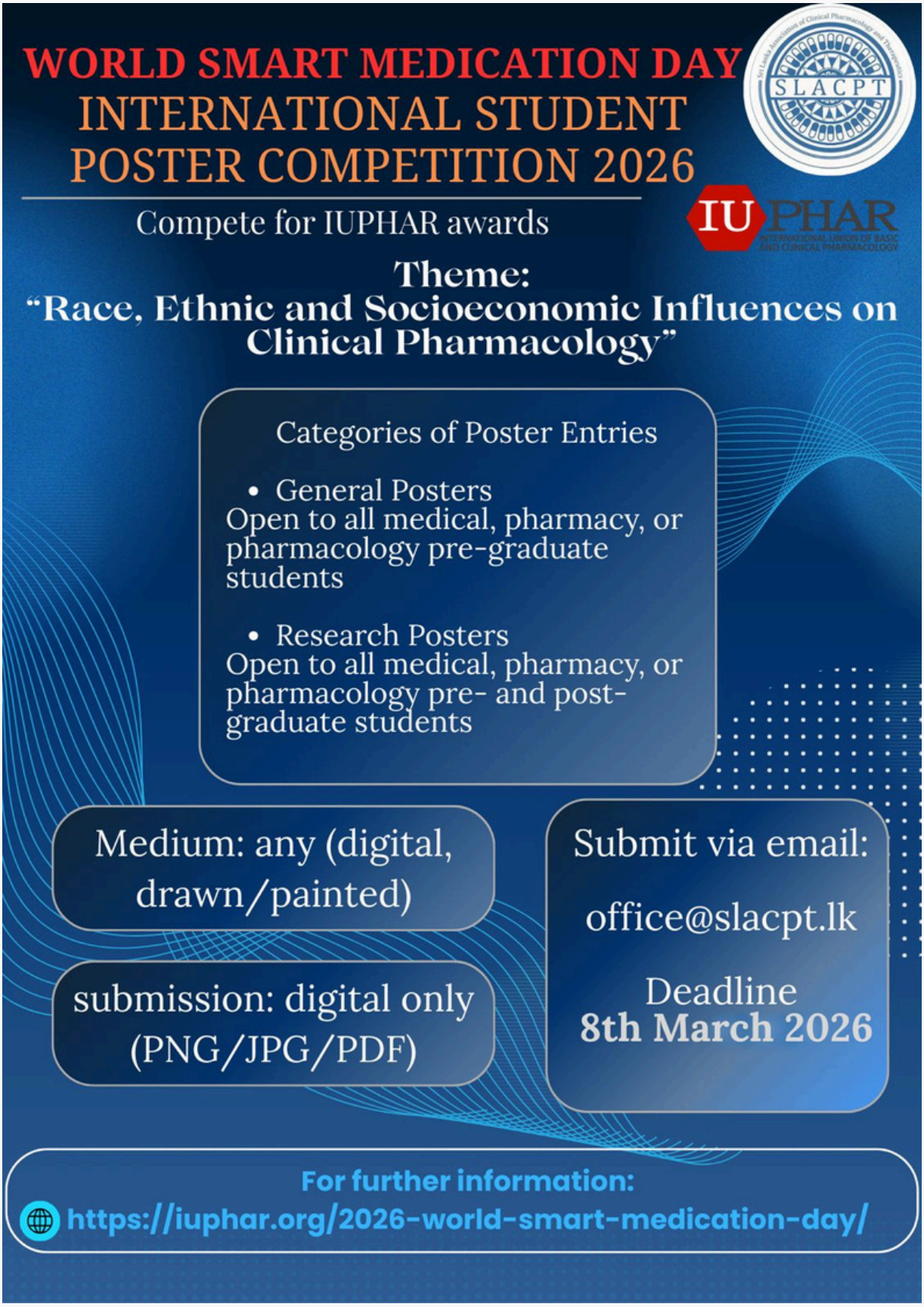

SLACPT NEWS

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