Quarter 3, 2025 | VOLUME 13 | NUMBER 9

Medical Bulletin

EXCEL Division of Blue Cross Laboratories Pvt Ltd.

UNDERSTANDING PROTON PUMP INHIBITOR'S (PPI's): REVIEW OF INDICATIONS AND COMPARATIVE ACID SUPPRESSION STRATEGIES

Since their introduction in 1989, proton pump inhibitors (PPIs) have become increasingly used worldwide for both therapeutic and prophylactic indications. PPIs inhibit the gastric H+/K+-ATPase enzyme system, the final step in acid secretion, offering more potent and sustained acid suppression than histamine-2 receptor antagonists (H2RAs). Their effectiveness and tolerability have established PPIs as some of the most frequently prescribed drug classes in primary care.

Proton pump inhibitors (PPIs) are among the most prescribed drugs worldwide owing to their proven efficacy in symptom control and mucosal healing for acid-related disorders including gastroesophageal reflux disease (GORD), peptic ulcer disease, Helicobacter pylori eradication, functional dyspepsia, and gastroprotection in high-risk patients.

In clinical practice, many acid-related disorders are initially managed with a finite course of PPIs ("treatment phase") followed by reassessment. For example, uncomplicated gastro-oesophageal reflux disease (GORD) or peptic ulcer disease is typically treated with a 4-8 week course to achieve mucosal healing and symptom resolution. After this induction period, clinicians should reassess the need for continued therapy.

Indications of PPI use:

Type of Indication	Long-Term PPI (>8 Weeks)	
	Definite	**Conditional**
Therapeutic	- GORD with erosive oesophagitis - Peptic stricture - Eosinophilic oesophagitis with histological response - Barrett's oesophagus - Zollinger-Ellison syndrome	- GORD with incomplete response to short-term PPI - GORD with recurrence of symptoms on PPI cessation - Eosinophilic oesophagitis (maintenance) - Idiopathic chronic cough (GORD-confirmed)
Prophylactic	- Chronic NSAID/aspirin use + high GI risk - Antiplatelet therapy post-bleeding ulcer - Systemic sclerosis with reflux	- Long-term corticosteroids + GI risk factors
	Short-Term PPI (<8 Weeks)	
Therapeutic	- GORD - *H. pylori* eradication (combination therapy) - Non-erosive GORD (symptom relief) - Peptic ulcer disease - Mild peptic inflammation	- Functional dyspepsia (trial) - Laryngopharyngeal reflux (LPR) (trial and review) - Mild gastritis

Type of Indication	Long-Term PPI (>8 Weeks)	
	Definite	Conditional
Prophylactic	- NSAID/aspirin use (short course + risk factors) - Post-endoscopic ulcer therapy - Stress ulcer prophylaxis (ICU only)	- Post-bariatric surgery (short-term) - Post-sclerotherapy and band ligation - To cover short-term NSAID/high dose steroid prescription

Summary of recommendation of different societies of PPI use with antiplatelet therapy

Organization	Guideline Summary
ACCF/ACG/AHA	PPIs are recommended for high-risk patients only on Dual Antiplatelet Therapy (DAPT) only. Routine use is not recommended.
ESC	Routine PPI use for all patients on DAPT.
International Consensus	Conditional recommendation for PPI in patients with previous ulcer bleeding on DAPT.
ANMCO/AIGO (Italian Guidelines)	PPI recommended for patients with GI risk factors, history of PUD, use of NSAIDs or steroids.

PPIs versus H2RAs, Gastroprotective Drugs and New Acid Suppressants

PPIs are typically preferred over cytoprotective agents and H2RAs according to European, British, and American guidelines. This preference is based on the superior effectiveness and safety profile of PPIs. New acid suppressants such as potassium-competitive acid blockers (PCABs) offer advantages over conventional PPIs.

Aspect	Guideline Summary	Notes
PPI Indications	PPIs are first-line treatment for GORD, peptic ulcer disease, and H. pylori eradication.	NICE and BSG recommend PPIs for GORD and ulcer healing.
Dosage and Duration	Standard dosing for GORD and ulcers. Long-term PPI use is common, especially in elderly patients.	Dosing varies based on severity; an annual review is recommended by the NHS to assess necessity.
Co-prescription with NSAIDs	NICE and BSG recommend co-prescription of PPIs with NSAIDs in high-risk patients (e.g., age > 65, history of ulcers, or anticoagulant use).	Reduces risk of GI bleeding, especially in patients on long-term NSAID therapy.
Co-prescription with Antiplatelet Therapy	PPIs should be prescribed for patients on DAPT or single therapy with additional GI risk factors (e.g., history of ulcers, *H. pylori*).	Prevents gastrointestinal bleeding in high-risk groups.

Aspect	Guideline Summary	Notes
Co-prescription with Anticoagulants	PPIs should be considered for patients on warfarin or direct oral anticoagulants (DOACs) at high risk of GI bleeding. Pantoprazole is preferred due to fewer drug interactions.	Particularly important for patients with prior GI bleeding or ulcer history.
Co-prescription with Corticosteroids	NICE recommends considering PPIs for high-risk patients on corticosteroids, particularly when combined with NSAIDs or other GI risk factors.	Focuses on reducing risk of peptic ulcers from corticosteroid use.
Deprescribing PPIs	NICE and NHS recommend annual reassessment of PPI use to reduce overprescription. PPIs should not be stopped in high-risk patients (GORD, Barrett's oesophagusesophagus).	Gradual tapering or continued use depending on clinical need.
Adverse Effects	Long-term PPI use is associated with risks such as gastrointestinal infections (C. *difficile*), nutrient deficiencies (B12, magnesium), and bone fractures.	NICE and NHS advise caution with long-term use; alternatives considered when appropriate.
Alternative Therapies	Sucralfate and misoprostol are alternatives for ulcer treatment, especially when PPIs are not suitable.	Cytoprotective agents and H2RAs as alternatives.
New Acid Suppressants	Potassium-competitive acid blockers (PCABs) like vonoprazan may offer advantages over traditional PPIs, particularly in PPI-resistant GORD and *H. pylori* eradication.	Emerging therapies are considered, but PPIs remain standard.

This outline shall support evidence-based overview of PPI indications, and promote appropriate, safer, and patient-centred use of acid-suppressive therapy.

Source: *Andrawes M, et.al; Harms, and Deprescribing. Medicina. 2025; 61(9):1569.*

ADDITIVE ANTI-INFLAMMATORY EFFECTS OF AMLODIPINE AND ATORVASTATIN IN ATHEROSCLEROSIS

Hypertension and dyslipidemia are two of the most commonly co-occurring cardiovascular important modifiable risk factors which together cause an increase in coronary heart disease-related events that is more than simply additive for anticipated event rates with each condition. However, treatment and control of combined hypertension and hypercholesterolemia are suboptimal.

Calcium channel blockers (CCBs) have been used for decades to treat hypertension, & Amlodipine is known to reduce the carotid intima-media thickness progression and the incidence of unstable angina and revascularization in patients with coronary artery disease (CAD). More recently, amlodipine demonstrated to

slow the progression of atherosclerosis and reduce cardiovascular events in patients with CAD and normal blood pressure (BP). These effects could be due to the special profile of amlodipine, which includes antioxidant, antiproliferative, and anti-inflammatory properties.

Statins are powerful drugs widely used in the treatment of cardiovascular diseases. Apart from their known hypolipemic properties, they have been reported to have pleiotropic effects, such as anti-inflammatory and immunomodulatory actions.

Atorvastatin (80 mg/day) decreased nuclear factor-κB (NF-κB) activation and monocyte chemoattractant protein-1 (MCP-1) expression in peripheral blood mononuclear cells, as well as macrophage infiltration in patients with carotid atherosclerosis.

Amlodipine and atorvastatin both have excellent efficacy and safety profiles for the treatment of hypertension and dyslipidemia, respectively. Clinical trials have shown that co-administration of these two agents, across the dose range, does not modify the efficacy of either medication. Given that statins and CCBs have different mechanisms of action, this synergic effect of lipid-lowering therapy and CCBs on human coronary atherosclerosis has been reported in the Regression Growth Evaluation Statin Study (REGRESS) trial.

Among the proposed vasculoprotective effects of this drug combination are their capacity to reverse endothelial dysfunction or to decrease oxidative stress. A potential synergistic and dose-dependent increase in nitric oxide release was too observed with combination treatment compared with individual components.

Hypertension is often associated with impaired fibrinolysis, usually expressed by increased levels of plasminogen activator inhibitor type 1 (PAI-1) and decreased activity of tissue plasminogen activator (t-PA); amlodipine and atorvastatin improved the fibrinolytic balance more than either single agent in hypertensive hypercholesterolemic patients with insulin resistance.

In the multicenter Atorvastatin and Amlodipine in Patients with Elevated Lipids and Hypertension (AVALON) trial more patients receiving combination therapy achieved their BP goal than patients receiving atorvastatin, and more patients receiving combination therapy achieved their LDL-C goal than patients receiving amlodipine. Similarly, significantly more patients receiving combination therapy achieved both their BP and LDL-C goals compared with those receiving single-agent therapy. The mean Framingham estimated 10-year CHD risk was significantly with combination therapy than with single-agent therapy.

Different studies in hypertensive hyperlipidemic patients have shown that the combination of atorvastatin and amlodipine has additive effects in the improvement of arterial compliance and in the fibrinolytic balance, early markers of vascular damage and atherosclerosis.

Collectively, the data available support the clinical antiatherosclerotic advantages of the concomitant use of CCBs and statins and, in particular, of atorvastatin with amlodipine beyond their established antihyperlipemic and antihypertensive modes of action.

Source: *José L. Martín-Ventura , et.al; Volume 74, Supplement 111, December 2008, Pages S71-S74 ;Madhuri D et.al; Vasc Health Risk Manag. 2009 May 21;5:377–387.*

EXCEL

Dr. Prabhu Kasture (MD, DPH)
Director Medical Services & Pharmacovigilance
Phone No.: 022-66638043
Email: prabhu.k@bluecrosslabs.com
Correspond: Blue Cross Laboratories Pvt Ltd., Peninsula Chambers, Ganpatrao Kadam Marg, Lower Parel, Mumbai 400 013.
Website: http://www.bluecrosslabs.com