# Amylin analogues: The missing piece in cardiometabolic care?

Written by The Life Science Feed Editorial Team · Published 25 September 2026 · Edited by Mara Voss

The complex relationship of glucose regulation, satiety, and energy expenditure defines cardiometabolic disease, a pervasive challenge in clinical practice. While incretin-based therapies have dominated recent advancements, the endogenous hormone amylin offers a distinct, yet complementary, physiological pathway that warrants deeper consideration for future therapeutic strategies.

Understanding amylin's role provides a foundation for exploring its therapeutic potential, particularly as we seek more comprehensive approaches to managing obesity, type 2 diabetes, and their cardiovascular sequelae. The journey from scientific rationale to clinical application for amylin analogues is a story of persistent investigation into fundamental metabolic control.

**KEY TAKEAWAYS**

- The Pivot: Amylin analogues offer a distinct mechanism of action, targeting satiety and glucose regulation through pathways complementary to GLP-1 agonists.
- The Data: Clinical development focuses on combination therapies, leveraging synergistic effects on weight loss and glycaemic control.
- The Action: Clinicians should monitor ongoing trials for amylin-based therapies, anticipating a new class that could offer enhanced benefits for patients with complex cardiometabolic needs.

Amylin, a 37-amino acid peptide hormone, is co-secreted with insulin from pancreatic beta cells in response to nutrient intake. Its physiological actions are broad, encompassing postprandial glucose regulation, gastric emptying modulation, and central nervous system effects on satiety. This endogenous hormone acts as a neuroendocrine brake on nutrient absorption and energy intake, a role distinct from, but synergistic with, insulin.

In individuals with type 1 and type 2 diabetes, amylin secretion is often deficient, mirroring the insulin deficiency. This observation provided the initial rationale for amylin replacement therapy, aiming to restore a vital component of normal metabolic regulation, with the stake being improved patient outcomes. Pramlintide, a synthetic amylin analogue, was the first therapeutic agent to emerge from this understanding, demonstrating modest but consistent benefits in glycaemic control and weight management.

## The Amylin Mechanism: Beyond Glucose

Amylin's primary mechanism involves slowing gastric emptying, which blunts postprandial glucose excursions. This effect is particularly valuable in diabetes management, where rapid glucose absorption often leads to hyperglycaemia. But amylin's influence extends beyond the gut, acting on specific receptors in the brainstem to enhance satiety and reduce

food intake. This central effect is critical for its role in weight management, offering a distinct pathway compared to other anti-obesity agents.

The hormone also suppresses postprandial glucagon secretion, further contributing to improved glucose homeostasis. This multi-pronged action on gastric emptying, satiety, and glucagon makes amylin a compelling target for cardiometabolic interventions. Its effects are not merely additive to insulin but address different facets of metabolic dysregulation, providing a more holistic approach to managing both glucose and weight.

Understanding these mechanisms is essential for appreciating the potential of next-generation amylin analogues and combination therapies, with the stake being the development of more effective treatments. The goal is to harness these physiological effects more potently and with improved tolerability, moving beyond the limitations of earlier compounds. The role of adipose tissue as a driver of cardiometabolic risk highlights the importance of therapies that address both weight and metabolic function.

But the challenge with early amylin analogues, such as pramlintide, lay in their relatively modest efficacy and the need for frequent injections, which limited broader adoption. The field recognized the need for compounds with enhanced pharmacological properties, including longer half-lives and greater receptor affinity, to unlock amylin's full therapeutic potential. This pursuit has led to the development of novel amylin mimetics and co-agonists.

## Combination Strategies: The Next Frontier

The true potential of amylin analogues may lie in their combination with other established metabolic therapies, particularly GLP-1 receptor agonists. GLP-1 agonists primarily enhance glucose-dependent insulin secretion, suppress glucagon, and promote satiety through different central pathways. The synergy between amylin and GLP-1 agonism is physiologically intuitive: one slows nutrient delivery, the other optimizes its processing and disposal, both contributing to reduced energy intake.

This combination approach aims to achieve greater weight loss and improved glycaemic control than either agent alone. Early clinical data from co-formulations or co-administered agents suggest that this synergistic effect is indeed achievable. Patients often experience more pronounced reductions in body weight and HbA1c, along with better control of postprandial glucose levels.

The development of dual agonists, targeting both amylin and GLP-1 receptors, represents a significant leap in this strategy. These single molecules are designed to activate both pathways simultaneously, potentially simplifying treatment regimens and enhancing patient adherence. The goal is to create a more potent and comprehensive metabolic intervention, addressing multiple facets of cardiometabolic disease with a single agent.

The success of GLP-1 agonists in weight management and diabetes has set a high bar, but the distinct, complementary actions of amylin suggest that combination therapies could offer superior outcomes for patients struggling with significant obesity and poorly controlled type 2 diabetes. For clinicians, this means a future where more powerful tools are available to tackle the complex pathology of these conditions, potentially moving beyond the current standard of care. The anti-inflammatory effects of GLP-1s also highlight a broader benefit that could be augmented by amylin's actions.

## Addressing Unmet Needs in Cardiometabolic Disease

Despite advances, significant unmet needs persist in cardiometabolic care. Many patients with obesity and type 2 diabetes do not achieve their treatment goals with existing monotherapies, often due to insufficient weight loss, persistent hyperglycaemia, or poor tolerability. Amylin-based therapies, particularly in combination, offer a new avenue to address these gaps.

For patients with high baseline body mass index and long-standing diabetes, the enhanced weight loss and glycaemic control observed with amylin co-agonists could be transformative. These therapies may provide a more effective option for those who have failed to respond adequately to GLP-1 monotherapy or other conventional treatments. The focus remains on improving patient outcomes, reducing cardiovascular risk, and enhancing quality of life.

The potential for amylin analogues to reduce the burden of cardiovascular events associated with obesity and diabetes is a key area of ongoing investigation. While direct cardiovascular outcome trials are still needed for novel amylin-based therapies, the significant improvements in weight, glucose, and lipid profiles suggest a beneficial impact on long-term cardiovascular health. This is a critical consideration for European GPs and specialists managing a patient population at high risk of cardiovascular morbidity and mortality, with the stake being improved patient survival and reduced healthcare burden.

The development pipeline for amylin-based therapies includes various formulations and combination approaches, reflecting the industry's commitment to exploring this pathway. As these agents progress through clinical development, clinicians will need to carefully evaluate their efficacy, safety, and place in the evolving treatment algorithm. The Oxford Handbook of Endocrinology and Diabetes remains an invaluable resource for staying current with these developments.

## Future Directions and Clinical Integration

The integration of novel amylin-based therapies into clinical practice will depend on several factors, including their demonstrated efficacy in large-scale trials, their safety profile, and their cost-effectiveness. Head-to-head comparisons with existing therapies, particularly GLP-1 agonists, will be essential to define their specific niche. The goal is not simply to add another drug to the armamentarium but to offer a genuinely superior or complementary option.

Patient selection will be important. Identifying subgroups most likely to benefit from amylin-based therapies, such as those with significant postprandial hyperglycaemia, pronounced insulin resistance, or a strong need for substantial weight loss, will optimize treatment outcomes. The convenience of administration, whether once-daily or once-weekly, will also play a role in patient adherence and overall treatment success.

The long-term safety data, particularly regarding gastrointestinal side effects, will be closely scrutinized. While amylin's mechanism naturally involves some gastrointestinal effects, managing these to ensure patient comfort and adherence is paramount. The clinical community will be looking for robust evidence that these new agents offer a favorable benefit-risk profile that justifies their adoption.

The ongoing research into amylin's broader metabolic effects, including its potential impact on lipid metabolism and inflammation, could further expand its therapeutic utility. As our understanding of cardiometabolic disease continues to evolve, therapies that target multiple interconnected pathways, like amylin, will become increasingly important.

The future of cardiometabolic care will likely involve more personalized and comprehensive approaches, with amylin analogues playing a significant role in that evolution.

**CLINICAL IMPLICATIONS**

The re-emergence of amylin as a therapeutic target, particularly in combination with GLP-1 agonism, signals a genuine shift in how we might approach complex cardiometabolic disease. For too long, we have treated components of the metabolic syndrome in isolation. These new agents, by hitting multiple pathways, offer a more integrated solution for patients struggling with both obesity and type 2 diabetes.

Clinicians should anticipate a new class of agents that could offer superior weight loss and glycaemic control compared to current monotherapies. This means a real opportunity to move more patients into remission or achieve more aggressive treatment targets, especially for those who have not responded adequately to GLP-1s alone. The enhanced satiety and gastric emptying effects of amylin could be particularly beneficial for patients with significant food cravings and postprandial glucose spikes.

But the practicalities of administration and potential gastrointestinal side effects will remain key considerations. While the greater efficacy is compelling, patient adherence hinges on tolerability. The industry must deliver not just potent molecules, but also formulations that are well-tolerated and convenient enough for long-term use in a chronic disease setting.

The long-term cardiovascular outcomes data for these novel amylin-based therapies will be the ultimate arbiter of their impact. While surrogate markers look encouraging due to observed improvements in weight and glucose, hard outcomes are what truly change practice. We need to see if these agents can translate improved weight and glucose into fewer heart attacks and strokes, cementing their place as a cornerstone of cardiometabolic risk reduction.

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## REFERENCES

1. 1. Kittelson KS, Junior AG, Fillmore N, da Silva Gomes R. Cardiovascular-kidney-metabolic syndrome - An integrative review. Prog Cardiovasc Dis. 2024;87:26-36. doi:10.1016/j.pcad.2024.10.012
2. 2. Peterseim CM, Jabbour K, Kamath Mulki A. Metabolic Syndrome: An Updated Review on Diagnosis and Treatment for Primary Care Clinicians. J Prim Care Community Health. 2024;15:21501319241309168. doi:10.1177/21501319241309168
3. 3. Huang PL. A comprehensive definition for metabolic syndrome. Dis Model Mech. 2009;2(5-6):231-7. doi:10.1242/dmm.001180
4. 4. Alkhulaifi F, Darkoh C. Meal Timing, Meal Frequency and Metabolic Syndrome. Nutrients. 2022;14(9). doi:10.3390/nu14091719
5. 5. Manta A, Georganta A, Roumpou A, et al. Metabolic syndrome in patients with schizophrenia: Underlying mechanisms and therapeutic approaches (Review). Mol Med Rep. 2025;31(5). doi:10.3892/mmr.2025.13479
6. 6. Chan JL, Masini I, Pisarska MD. Polyendocrine metabolic ovarian syndrome (PMOS)/polycystic ovary syndrome (PCOS): current and future trends. J Clin Invest. 2026;136(12). doi:10.1172/JCI202824

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