Clinical Case Reports and Studies
2026 Volume 12, Issue 5
DOI: 10.59657/2837-2565.brs.26.323

BioRes Scientia
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Opinion Article

Open Access

Semaglutide in India: A Critical Inflection Point-An Opinion

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The Post-Patent Era of Semaglutide in India

The evolving intellectual property (IP) landscape surrounding semaglutide represents a critical juncture for healthcare in India. Originally developed by Novo Nordisk, semaglutide has rapidly transitioned from a therapy for type 2 diabetes (T2D) to a broader metabolic intervention, redefining the clinical management of diabetes and obesity [1,2]. With patent protections expiring in March 2026 in India, the country is currently facing a pivotal question: how should a powerful, system-wide metabolic regulator be integrated into its diverse and resource-variable healthcare ecosystem? Semaglutide's clinical impact arises from its function as a long-acting analog of glucagon-like peptide-1 (GLP-1), a hormone essential for metabolic homeostasis [3,4] By activating GLP-1 receptors (GLP-1R) in the pancreas, gastrointestinal (GI) tract, and central nervous system (CNS), it enhances glucose-stimulated insulin secretion, suppresses glucagon release, delays gastric emptying, and reduces appetite via hypothalamic pathways [5]. These effects translate into improved glycemic control (reduction in glycated hemoglobin [HbA1c]), weight loss, and cardiovascular (CV) risk reduction in individuals with T2D and obesity. Beyond established metabolic outcomes, emerging evidence suggests potential modulation of biological processes associated with aging, including chronic low-grade inflammation ("inflammaging"), oxidative stress, mitochondrial dysfunction, and cellular senescence [6]. Early clinical and preclinical findings indicate that GLP-1R activation may be associated with favorable shifts in biological aging markers and reduced risk of age-related diseases [7,8]. However, these observations are based on indirect, associative, and early-stage evidence and should not yet be interpreted as proof of causal healthspan extension.

Consequently, semaglutide may serve as a systemic regulator of healthspan rather than merely a disease-specific treatment, although long-term validation is still insufficient. These observations naturally raise an important clinical question: should individuals without overt metabolic disease consider such therapies for healthspan enhancement? While GLP-1 receptor agonists (GLP-1 RAs) align with preventive and optimization-oriented medicine, extending their use to healthy populations introduces uncertainties due to limited long-term safety data in such contexts. In the absence of disease, the benefit–risk balance becomes less clear, and concerns regarding overmedicalization, cost, weight regain after discontinuation, and inequitable access become more pronounced. Thus, although conceptually attractive, the use of semaglutide for healthspan extension in non-diabetic and non-obese individuals remains clinically premature and ethically complex. This question is of paramount importance, as the accessibility of generic semaglutide is becoming increasingly evident in India, and cost is no longer a major barrier in the growing pursuit of "healthspan" or "longevity extension" [9,10].

Importantly, this broad spectrum of activity is enabled by deliberate molecular engineering. Semaglutide is a modified 31-amino acid GLP-1R agonist with approximately 94% homology to native GLP-1. It is designed to overcome the rapid degradation of endogenous GLP-1, which has a half-life of 1-2 minutes due to dipeptidyl peptidase-4 (DPP-4)-mediated cleavage, resulting in a prolonged elimination half-life of approximately one week [11,12]. Structural modifications include substitution of alanine at position 8 with aminoisobutyric acid (Aib) to confer DPP-4 resistance, replacement of lysine at position 34 with arginine, and attachment of a C18 fatty diacid side chain via a hydrophilic spacer at lysine 26 [13,14]. This promotes reversible albumin binding, reduces renal clearance, and enables sustained systemic exposure with once-weekly dosing. While these features enhance clinical utility, they also increase manufacturing complexity and formulation sensitivity.

In contrast, the entry of generic or follow-on versions-more accurately described as complex generics or peptide therapeutics with biosimilar-like considerations in the Indian regulatory context-introduces a critical branded-generic divide. Branded semaglutide benefits from extensive clinical trial evidence, stringent manufacturing standards, and well-characterized safety and efficacy profiles. In contrast, peptide therapeutics are highly sensitive to variations in synthesis, folding, purification, and formulation, which may influence pharmacokinetics (PK), pharmacodynamics (PD), bioavailability, and immunogenicity [15,16]. This underscores the need for rigorous comparability frameworks rather than conventional bioequivalence alone, along with strengthened regulatory oversight. Drug stability further complicates real-world deployment. As a peptide-based therapeutic, semaglutide is vulnerable to degradation due to temperature fluctuations, oxidation, and aggregation. While branded formulations are optimized for controlled supply chains, replicating such stability in follow-on products remains challenging, particularly in settings with variable cold-chain infrastructure such as India [17]. Injectable formulations are especially sensitive to storage conditions, whereas oral formulations, though still requiring stability control, are comparatively less dependent on strict cold-chain logistics. In this context, branded products may retain an advantage through consistent quality assurance, stability under real-world conditions, and robust clinical evidence, although affordability considerations and policy interventions such as subsidies may help improve access.

Despite these challenges, expanded access to semaglutide could yield substantial public health benefits in India, where diabetes and obesity constitute a growing dual burden across urban and rural populations. Improved access may enable earlier intervention, reduce complications, and support a shift toward preventive metabolic care. However, this potential must be interpreted within a nuanced biological and epidemiological context. The obesity paradox suggests that higher body mass index (BMI) may, in certain populations, correlate with improved survival, particularly among older adults and those with chronic disease, although causality remains debated and context-dependent [18,19]. In India, where undernutrition and overnutrition coexist, indiscriminate weight loss may lead to unintended consequences such as sarcopenia, frailty, and metabolic instability, emphasizing the need for individualized treatment approaches rather than uniform weight-centric strategies [20,21]. Further complexity arises from semaglutide's pharmacological profile. Unlike endogenous GLP-1, which is released transiently in a pulsatile manner, semaglutide produces sustained receptor activation, enhancing efficacy but also increasing the likelihood of adverse effects such as gastrointestinal (GI) symptoms (nausea, vomiting) [22]. Additional concerns include gallbladder-related events and debated associations with pancreatitis, although causal relationships remain inconclusive. These risks may be amplified in real-world settings with limited monitoring, particularly in rural India, where healthcare access, diagnostic capacity, and longitudinal follow-up remain uneven. While lower-cost formulations may improve access and reduce disparities, limited clinical oversight may increase the risk of inappropriate or unsupervised use, including for non-medical or cosmetic purposes, and in populations with undernutrition, anemia, or sarcopenia, such use may further worsen outcomes.

These dynamics reflect a broader phenomenon: the medicalization of lifestyle. As pharmacological interventions become more accessible, there is a potential shift away from sustained behavioral strategies such as diet and physical activity. From an economic perspective, moral hazard may emerge if individuals perceive medication as a substitute for healthy behaviors, potentially undermining long-term metabolic resilience, particularly in younger populations [23]. Moreover, beyond these societal considerations, India also faces a strategic decision regarding its role in the global pharmaceutical ecosystem-whether to remain primarily a generic manufacturing hub or to invest more actively in innovation-driven therapeutics. While generics offer affordability and scalability, they limit control over intellectual property and innovation. In contrast, developing indigenous branded peptide therapeutics could strengthen scientific leadership and long-term competitiveness, although this requires substantial investment, advanced infrastructure, and sustained policy support. A hybrid approach that leverages strengths in generics while selectively investing in innovation ecosystems may provide a balanced pathway.

In essence, the introduction of semaglutide thus represents more than a pharmaceutical transition; it constitutes a system-level stress test for India's

healthcare infrastructure serving a population of 1.4 billion, particularly amid brand overcrowding, with as many as more than 40 Indian companies releasing semaglutide in the market, thereby increasing decision complexity and regulatory burden. Regulatory frameworks must evolve to address the unique challenges of peptide therapeutics, including stringent manufacturing standards, robust comparability criteria, and comprehensive pharmacovigilance systems, while ethical deployment should prioritize clinical need over market-driven or aesthetic demand. National-level monitoring systems, such as those coordinated by the Indian Council of Medical Research (ICMR), can support real-world evidence generation and inform policy. More importantly, government subsidies for branded, patent-protected semaglutide could potentially lower costs and narrow the price gap with generics, while also encouraging Indian manufacturers to maintain high standards for their generic products. If integrated thoughtfully, affordable access through public healthcare systems could improve equity and population health outcomes, provided appropriate safeguards ensure quality, monitoring, and rational use across diverse healthcare settings.

Taken together, semaglutide exemplifies the intersection of molecular precision and clinical ambition; however, its broader significance lies in the insights it offers into healthcare priorities, raising the central question of whether India can leverage this innovation to promote equitable, preventive care or whether it may inadvertently reinforce patterns of overmedicalization and inequity. The key issue is not the efficacy of semaglutide, which is well established, but how its integration into the healthcare system can be guided by principles of equity, sustainability, and long-term public health impact. If properly integrated, it has the potential to significantly reduce the economic burden associated with managing a wide range of chronic diseases affecting large segments of the population, particularly those linked to overweight, obesity, and metabolic syndrome. Furthermore, given the pleiotropic benefits of GLP-1–based drugs across multiple conditions, including mental health, generic semaglutide offers a low-cost approach to managing a broad spectrum of diseases [24,25]. This includes not only symptomatic relief but also potential disease-modifying effects. Thus, it is critical to capitalize on India's worldwide recognition as the "pharmacy of the world" and leverage this strength to support the health of a large, age-diverse population, ultimately enhancing workforce productivity and contributing to economic growth while positioning India as a key benchmark in the adoption and accessibility of GLP-1-based therapies. In this context, the expanding use of generic weight loss drugs represents a watershed moment for India—not merely as a clinical advance, but as a broader societal inflection point that will shape how the nation defines health, equity, and well-being in the years to come.

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Declarations

Conflict of Interest

The author does have anything to declare.

Funding

None.

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Cite this article: Chakrabarti SK. (2026). Semaglutide in India: A Critical Inflection Point-An Opinion, *Clinical Case Reports and Studies*, BioRes Scientia Publishers. 12(5):1-11. DOI: 10.59657/2837-2565.brs.26.323

Article History: **Received:** April 01, 2026 | **Accepted:** April 22, 2026 | **Published:** April 29, 2026