Clinical Pearls of Choosing the Right Semaglutide Brand in Diabetes: Indian Real-world Case Series

Choosing the Right Semaglutide Brand: Indian Real-world Cases

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ABSTRACT

Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as semaglutide, play a pivotal role in helping patients manage type 2 diabetes mellitus (T2DM) and obesity by improving glycemic control, supporting weight reduction, and enhancing appetite regulation. With the recent launch of generic semaglutide brands, clinicians now have multiple prescribing options. There are currently no real-world case studies of switching among these brands in India.

Methods: We present four Indian real-world case reports involving patients with T2DM and/or weight issues who were transitioned between semaglutide brands. Key clinical parameters, patient-reported outcomes, treatment adherence, and device usability were assessed before and after the switchover, with short-term follow-up.

Results: In these cases, switching between semaglutide brands was associated with clinically relevant challenges, including differences in efficacy, gastrointestinal tolerability, appetite control, device usability, and treatment adherence. These differences contributed to early variations in glycemic control, body weight, and caregiver support dependence in some patients. In all these cases, patients expressed a preference for the reference semaglutide brand (Ozempic® or Rybelsus®), citing greater tolerability, better control, familiarity, and ease of use.

Conclusion: These cases highlight the clinical significance of brand-related and device-related factors in determining therapeutic outcomes with semaglutide. Careful consideration of patients' experience, device familiarity, and close monitoring following treatment switches helps optimise adherence and clinical efficacy in routine Indian clinical practice.

Keywords- Glucagon-like peptide-1 receptor agonists, semaglutide, type 2 diabetes mellitus, obesity, weight loss, Ozempic®, Rybelsus®

INTRODUCTION

Diabetes represents a major global health challenge and imposes a substantial economic burden on India. According to the Indian Council of Medical Research–India Diabetes (ICMR-INDIAB) study (2023), nearly 101 million individuals are currently living with diabetes, a number projected to increase to approximately 124.9 million by 2045, according to the International Diabetes Federation (IDF) Diabetes Atlas [1,2]. Weight issues play a significant role in driving the type 2 diabetes mellitus (T2DM) epidemic, with nearly 88% of individuals with T2DM classified as overweight or obese [3].

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are widely used in the management of T2DM due to their ability to improve glycemic control, support weight loss, provide long-term organ protection and carry a low risk of hypoglycemia [4,5]. Semaglutide is a long-acting GLP-1-RA indicated for the management of T2DM and chronic weight management, in addition to other approved indications. Developed originally by Novo Nordisk, it is manufactured using recombinant DNA (rDNA) technology, with modifications to incorporate an N-terminal oligopeptide and a C18 fatty acid side chain [6]. With the loss of exclusivity of the semaglutide patent in India (in March 2026), there has been an influx of multiple semaglutide brands. All generic injectable semaglutide brands for diabetes management (copies of Ozempic®) are synthetic and not manufactured using time-tested rDNA technology [7,8]. However, these alternative manufacturing approaches may alter the clinical characteristics of the product [9]. Recent evidence shows that semaglutide produced by different manufacturers or processes can have significantly different impurity profiles, stability concerns, reduced active pharmaceutical ingredient (API) content, and potential immunogenic risk. These alterations may impact the efficacy and safety of the product [9,10].

Similarly, there are follow-on brands of oral semaglutide (Rybelsus®) also available in the Indian market. Unlike injectable copies, these oral copies are manufactured either synthetically or via rDNA origin. However, differences in the composition or concentration of the absorption enhancer exist between Rybelsus® and the other brands. These subtle differences could potentially lead to variations in clinical outcomes since the innovator company has spent over 15 years identifying the right absorption enhancer chemistry and concentration (300 mg of sodium N-[8-{2-hydroxybenzoyl} amino] caprylate [SNAC] for Rybelsus® strengths of 3 mg, 7 mg and 14 mg) [11,12]. In this narrative case series, the authors present real-world experiences in India of switching between innovator semaglutide brands (Ozempic® or Rybelsus®) and generic semaglutide brands for T2DM management. The paper focuses on differences in clinical outcomes and tolerability, following such transitions in routine practice.

CASE SERIES

Case 1: Early Loss of Glycaemic Stability Following Switch from Original to Synthetic Semaglutide (injectable)

A 58-year-old North Indian man with a 9-year history of T2DM, along with hypertension and dyslipidemia, presented for routine glycemic management. At baseline, his diabetes was suboptimally controlled, with a glycated hemoglobin (HbA1c) of 8.6% and a fasting plasma glucose (FPG) of 168 mg/dL. He was obese, weighing 92 kg with a body mass index (BMI) of 31.2 kg/m², and also had elevated blood pressure and a deranged lipid profile, including raised low-density lipoprotein (LDL) cholesterol, low high-density lipoprotein (HDL) cholesterol, and mildly elevated triglycerides (Table 1).

Table 1. Baseline Clinical Parameters (Pre-semaglutide Initiation)

Parameter	Value
HbA1c	8.6%
FPG	168 mg/dL
Body weight	92 kg
BMI	31.2 kg/m²
Blood pressure	142/88 mmHg
LDL-C	132 mg/dL
HDL-C	38 mg/dL
Triglycerides	162 mg/dL

At baseline, the patient was on Metformin 1 g twice daily, Empagliflozin 10 mg once daily (OD), Telmisartan 40 mg OD, and Rosuvastatin 10 mg OD.

In view of inadequate glycemic control and excess body weight, the patient was initiated on once-weekly reference injectable semaglutide (Ozempic®) with standard dose escalation, starting at 0.25 mg weekly, then 0.5 mg weekly, and finally 1 mg weekly over a period of 3 months. After 3 months of treatment, the patient achieved marked clinical improvement. His HbA1c decreased to 6.7%, FPG improved to 112 mg/dL, and body weight reduced to 85 kg. The patient also experienced improved blood pressure control and lipid parameters (Table 2). These objective improvements were accompanied by a pronounced reduction in appetite and better satiety, which supported sustained dietary control. The patient also reported reduced cravings for fast food and junk food, suggesting some level of elimination of 'food noise'.

Table 2. Clinical Outcomes After 3 Months of Reference Semaglutide Therapy

Parameter	Value
HbA1c	6.7%
FPG	112 mg/dL
Body weight	85 kg (−7 kg)
Blood pressure	130/82 mmHg
LDL-C	94 mg/dL
Triglycerides	152 mg/dL

Due to cost considerations, the patient was subsequently switched from reference semaglutide to a synthetic semaglutide brand at the same 1 mg weekly dose. Within 4 weeks after switching, an early deterioration in metabolic stability was observed. FPG increased to 131 mg/dL, and body weight increased by 2 kg. The patient also reported a noticeable reduction in appetite suppression compared with the period on the reference product, with larger portion sizes and more food intake (Table 3).

Table 3. Clinical Status 4 Weeks After Switch to Synthetic Semaglutide Brand

Parameter	Value
FPG	Increased from 112 to 131 mg/dL (+19 mg/dL)
Body weight	Increased from 85 to 87 kg (+2 kg)
Blood pressure	134/84 mmHg

Given the early loss of glycemic control, weight regain, and reduced satiety following the switch, the treating physician and the patient mutually decided to revert to the reference semaglutide brand. This case illustrates the potential clinical impact of switching between semaglutide brands on glycemic control, weight regulation, and appetite modulation, and further highlights the importance of close clinical monitoring when therapeutic substitutions are made, particularly for patients who have achieved stable metabolic control.

Case 2: Early Gastrointestinal Tolerability Differences Following Switch from Original to Synthetic Semaglutide (injectable)

A 47-year-old South Indian woman with T2DM, obesity and hypertension presented for optimisation of glycemic control. At baseline, she had sub-optimal glycemic control, obesity, elevated blood pressure, and an unfavourable lipid profile (Table 4).

Table 4. Baseline Clinical Parameters (Pre-semaglutide Initiation)

Parameter	Value
HbA1c	**8.1%**
FPG	**150 mg/dL**
Body weight	**94 kg**
BMI	**34 kg/m²**
Blood pressure	**136/86 mmHg**
LDL-C	**118 mg/dL**
HDL-C	**41 mg/dL**
Triglycerides	**198 mg/dL**

At baseline, the patient was receiving metformin 500 mg twice daily, sitagliptin 100 mg OD, and amlodipine 5 mg OD. Sitagliptin was discontinued, and she was initiated on once-weekly reference semaglutide (Ozempic®), which was slowly titrated over 3 months to 1 mg weekly and was well tolerated, except for mild, transient nausea during dose escalation (resolved within approximately 3 days after each dose increment). After 3 months of treatment, she demonstrated significant clinical improvement, including a reduction in HbA1c to 6.3%, weight loss of 8 kg, improved blood pressure, and better lipid parameters (Table 5).

Table 5. Clinical Outcomes After 3 Months of Reference Semaglutide Therapy

Parameter	Value
HbA1c	**6.3%**
FPG	**108 mg/dL**
Body weight	**86 kg (−8 kg)**
Blood pressure	**128/80 mmHg**
LDL-C	**90 mg/dL**
Triglycerides	**150 mg/dL**

Subsequently, at the patient's request, therapy was switched to a synthetic semaglutide brand at the same dose of 1 mg once weekly. Within 3 days of the switch, the patient experienced worsening gastrointestinal intolerance, including persistent nausea, vomiting, and diarrhea, leading to one missed dose. This was accompanied by early signs of deterioration in glycemic control, with higher FPG levels and slight weight regain (Table 6). The dose was then reduced to 0.5 mg weekly to enable better gastrointestinal tolerance. However, the patient continued to experience severe vomiting even with the reduced dose. Due to this poor tolerability and declining therapy adherence, the patient requested to switch back to the reference brand.

Table 6. Clinical Parameters 3 Weeks After Switch to Synthetic Semaglutide Brand

Parameter	Value
Body weight	**87 kg (+1 kg)**
FPG	**Increased from 108 to 122 mg/dL (+14 mg/dL)**
Blood pressure	**130/82 mmHg**

This case highlights the potential for variation in gastrointestinal tolerability following a switch between semaglutide brands, which may ultimately affect patient adherence, short-term glycemic outcomes, and overall treatment persistence. It emphasises the need for close monitoring of tolerability and adherence when transitioning between brands, particularly in therapies where gastrointestinal effects are dose-limiting.

Case 3: Impact of Device Usability on Adherence Following Switch from Original to Synthetic Semaglutide (injectable)

A 63-year-old man from West India with a 12-year history of T2DM complicated by peripheral neuropathy presented for glycaemic review. At baseline, he had poor glycemic control and elevated blood pressure (Table 7), while on treatment with metformin 1 g twice daily, sitagliptin 100 mg OD, insulin degludec 12 units at bedtime and pregabalin 75 mg at bedtime.

Table 7. Baseline Clinical Parameters (Pre-semaglutide Initiation)

Parameter	Value
HbA1c	**8.8%**
FPG	**168 mg/dL**
Body weight	**84 kg**
Blood pressure	**146/90 mmHg**

He was initiated on once-weekly semaglutide (Ozempic®, titrated to the maintenance dose of 1 mg weekly) using the Novo Nordisk pen device, with which he was already familiar from prior insulin use with the same company. Over 3 months, he demonstrated significant improvements in glycemic control (HbA1c reduced to 6.9%, FPG to 112 mg/dL), weight reduction (−6 kg), and better cardiometabolic parameters, with good adherence (Table 8). Furthermore, the dose of degludec was also reduced to 8 units daily, and sitagliptin was discontinued.

Table 8. Clinical Outcomes After 3 Months of Reference Semaglutide Therapy

Parameter	Value
HbA1c	**6.9%**
FPG	**112 mg/dL**
Body weight	**78 kg (−6 kg)**
Blood pressure	**134/84 mmHg**

Subsequently, he was switched to a locally available synthetic semaglutide brand that utilises a different pen device. Over the next 4 weeks of this switch, the patient reported multiple device-related challenges, including difficulty with the dose dial mechanism, in which he was unable to visualize the displayed dose in the window. Also, he felt that the force required to inject the semaglutide dose was significantly higher than with the Novo Nordisk pen, which meant that he had to rely on his wife or son to administer the dose to him. These practical issues contributed to reduced adherence and possible microdosing, leading to a rise in fasting glucose levels (from 112 to 138 mg/dL) and slight weight gain (Table 9).

Table 9. Clinical Status 4 Weeks After Switch to Synthetic Semaglutide Brand

Parameter	Value
FPG	**Increased from 112 to 138 mg/dL (+26 mg/dL)**
Body weight	**Increased from 78 to 80 kg (+2 kg)**
Blood pressure	**134/84 mmHg**

Owing to the cumbersome nature of drug administration, the patient expressed a desire to switch back to the original brand, citing quality and familiarity with the device, and improved ease of use. He chiefly opted for this switch-back as he did not want to rely on his caregivers for drug administration.

This case underscores the critical role of the drug–device interface in chronic injectable therapies, which is typically ignored or overlooked in the clinical setting. Variations in device design or quality may affect patient confidence and usability, lead to administration errors, and ultimately impact adherence and metabolic outcomes. It highlights the importance of considering ease of use and training requirements when switching between injectable brands, particularly in elderly patients or those with comorbidities that impair dexterity or cognition.

Case 4: Loss of Metabolic Control Following Switch from Original to Generic Semaglutide (oral)

A 42-year-old woman from South India, newly diagnosed with T2DM, presented for metabolic care (weight and glucose optimisation). At baseline, she had sub-optimal glycemic parameters and also battled with weight-related challenges. (Table 10).

Table 10. Baseline Clinical Parameters (Pre-semaglutide Initiation)

Parameter	Value
HbA1c	**7.8%**
FPG	**155 mg/dL**
Body weight	**82 kg**
BMI	**27 kg/m²**
Blood pressure	**112/64 mmHg**

The patient was advised to start semaglutide therapy as a first-line diabetes management option. Since she was reluctant to initiate injectable therapies, the treating physician offered the reference oral semaglutide brand (Rybelsus®). The patient agreed to initiate therapy with oral semaglutide after understanding the clinical benefits. The dose was initially 3 mg daily, slowly titrated over the next month to 7 mg daily and then to the higher dose of 14 mg for glycemic control and, additionally, weight management. The patient had transient episodes of nausea (without vomiting) when the dose was up-titrated to 14 mg. Treatment resulted in substantial weight reduction and improved glycemic control, accompanied by effective appetite suppression and early satiety. The clinical outcomes after 3 months of intervention are presented in Table 11.

Table 11. Clinical Outcomes After 3 Months of Reference Semaglutide Therapy

Parameter	Value
Body weight	**74 kg (−8 kg)**
HbA1c	**6.1%**
FPG	**Reduced from 155 to 98 mg/dL (-57 mg/dL)**

On the patient's request to optimize prescription costs (after she had seen news articles about brands available at lower monthly costs), she was switched to a generic oral semaglutide at a 1:1 dose switch (14 mg OD). Initially, the patient reported a burning sensation in the stomach, which was managed with pantoprazole 40 mg OD. Within 2 weeks of the switch, the patient reported a noticeable decline in appetite control, including increased thoughts about food, reduced early satiety, return of evening cravings, and larger portion sizes. Clinically, this was associated with early weight regain and increased fasting glucose (Table 12).

Table 12. Clinical Parameters 4 Weeks After Switch to Generic Oral Semaglutide Brand

Parameter	Value
Body weight	**Increased from 74 to 76 kg (+2 kg)**
FPG	**Increased from 98 to 114 mg/dL (+16 mg/dL)**

In view of these changes, the patient opted to resume therapy with the original brand.

This case illustrates the potential impact of switching between semaglutide brands on central appetite regulation and satiety signaling, which represent key therapeutic effects of GLP-1 RAs. The observed changes highlight that appetite control serves as a sensitive and early indicator of therapeutic response, while variability in clinical effect may influence both weight trajectory and glycemic outcomes. These findings underscore the need for close monitoring following treatment substitution, particularly in patients in whom weight loss is an important therapeutic goal.

DISCUSSION

The original semaglutide molecule has been developed and manufactured by Novo Nordisk. It is available in subcutaneous and oral formulations for diabetes management, under the brand names of Ozempic® and Rybelsus®, respectively [13]. Semaglutide is a structurally modified analogue of human GLP-1, indicated for the management of T2DM, among other clinical indications. GLP-1 RAs exert their effects by binding to GLP-1 receptors distributed across multiple organ systems. Centrally, they act on the brain to reduce appetite; in the gastrointestinal tract, they delay gastric emptying, collectively contributing to weight reduction as an additional clinical benefit in people with T2DM [14].

Early-phase 2 and phase 3a clinical trials of semaglutide were designed to determine the optimal dosing regimen and assess its safety and efficacy in individuals with T2DM. Subsequent large-scale clinical programmes further confirmed the efficacy and safety of both subcutaneous and oral formulations in the management of T2DM. Over time, the indications for subcutaneous semaglutide were expanded to include chronic weight management in individuals with obesity or overweight, particularly those with comorbidities such as diabetes, hypertension, dyslipidemia, obstructive sleep apnoea, cardiovascular disease (CVD), and osteoarthritis. Moreover, it has demonstrated benefits on cardiovascular and renal outcomes, as well as the ability to improve glycemic control and promote clinically meaningful weight loss. It has approved label indications for use in diabetes patients with CVD and/or chronic kidney disease (CKD) for reducing the risk of adverse cardiac and renal outcomes [11,12,15]. The premium wall of evidence available with the original brands now exceeds 50 clinical trials, with significant Indian representation. On the other hand, generic brands of semaglutide for T2DM have been studied in Phase 3 trials for only 24–26 weeks in small groups of participants (mostly 100–200). Furthermore, the generic brands have not been studied in dedicated cardiovascular, renal or arterial outcomes trials (as with SUSTAIN 6, PIONEER 6, SOUL, FLOW or STRIDE with the original brands). Regarding oral semaglutide brands, it is critical to note that the appropriate concentration of SNAC is essential for adequate absorption and bioavailability. When the SNAC concentration is suboptimal (~160 mg in generic brands), the clinical data for Rybelsus® cannot be extrapolated [11,12,15].

These clinical observations suggest that generic brands of semaglutide may not always replicate the full therapeutic performance or provide similar safety as the original formulations. A plausible explanation lies in the inherent variability between the originator and copy products. Differences in manufacturing processes, production scale, equipment, host systems, and raw materials can lead to physicochemical variability, even when the peptide sequence remains the same. Additionally, the method of synthesis, recombinant versus chemical, may influence the final product characteristics.

Supporting this, evidence from case studies indicates that semaglutide produced by different manufacturers or through different techniques can exhibit distinct impurity profiles [8]. Similar findings have been reported by Hach M *et al*., who found that comparative analyses of follow-on semaglutide and liraglutide products versus their originators demonstrated differences in impurity composition, potential stability concerns, reduced API content, and possible immunogenic risks [10].

In this context, pharmaceutical stability assumes even greater importance, as it directly impacts drug safety, efficacy, and consistency over the product lifecycle. Environmental factors such as temperature, humidity, and light can accelerate degradation, particularly in tropical and resource-limited settings where infrastructure constraints and climatic variability pose additional challenges [16]. Climate change–related disruptions, including floods and power outages, may further compromise storage conditions and supply chains [17]. For temperature-sensitive therapies such as semaglutide, strict adherence to cold-chain requirements (2–8°C) is critical, as even brief temperature excursions during transport or storage can affect product integrity. Continuous monitoring using data loggers and real-time tracking, along with robust cold-chain logistics, is therefore essential. The stringent storage requirements of semaglutide further highlight the advantage of established manufacturers (such as Novo Nordisk) with long-standing expertise in cold-chain management, ensuring consistent product quality across distribution [18–20].

It is also important to remember that drug delivery devices are integral to injectable semaglutide therapy, as they affect dosing accuracy, ease of use, and patient confidence. Prefilled pen devices from established manufacturers are widely preferred due to their reliability and user familiarity. Modern designs incorporate features such as spring-assisted mechanisms, clear dose displays, end-of-dose confirmation, and color coding, which enhance usability, reduce errors, and improve patient confidence. Accurate and consistent dose delivery remains essential, particularly for peptide therapies with dose-dependent effects. User-friendly devices are especially beneficial for elderly patients or those with limited dexterity, as they support ease of use and adherence. Although device design alone does not determine clinical outcomes, it is an important practical factor that, along with drug quality and clinical evidence, can improve treatment acceptance, long-term adherence, and overall disease management [21,22].

Taken together, these insights provide a mechanistic basis for the observed clinical variability and reinforce the need for caution, close monitoring, and informed decision-making when considering non-medical switching in patients who are stable on semaglutide therapy.

CONCLUSION

Reference or original semaglutide provides comprehensive metabolic benefits in patients with T2DM, going beyond glucose-lowering alone. This case series demonstrates that the right choice of semaglutide brand is an important factor associated with significant improvements in glycemic control (HbA1c), body weight, blood pressure, and lipid parameters, highlighting its role in holistic cardiometabolic risk reduction. This compilation of four real-world cases suggests that Ozempic® and Rybelsus®, as the reference semaglutide brands, continue to be the 'gold standard' semaglutide options in Indian T2DM practice. The synthetic brands of semaglutide launched in India have shown variable clinical outcomes in the cases highlighted in this publication. Clinicians need to consider these differences before making informed choices of the semaglutide brand in routine practice.

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