VIEWPOINT

Pragmatic Considerations in Switching to Semaglutide for Obesity Management: Real-World Perspectives

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ABSTRACT

Incretin-based therapies have transformed the management of obesity and related cardiometabolic diseases. With the increasing availability of agents such as semaglutide and tirzepatide, switches between therapies are occurring in clinical practice despite the absence of formal randomized evidence guiding such transitions. This review outlines pragmatic, experience-based considerations for switching from tirzepatide to semaglutide including clinical rationale, dose conversion approaches, titration strategies, and cost-sensitive implementation. These practical insights aim to support clinicians in optimizing individualized, safe, and cost-effective obesity management.

Keywords: Obesity, switching, semaglutide, tirzepatide, dose conversion, guidance, individualized care

The global burden of obesity continues to rise, driving increased utilization of incretin-based pharmacotherapies[1]. Semaglutide and tirzepatide represent two efficacious pharmacologic interventions currently available for chronic weight management; both having dose-dependent weight loss effect. With their respective highest approved doses by the US Food and Drug Administration (US FDA), in obesity without diabetes, the weight loss effect of tirzepatide between 16.0% to 22.5% (5-15 mg) and that of semaglutide is between 18.2% to 20.7% (2.4-7.2 mg)[2-4].

In addition to magnitude of weight loss, quality of weight loss has also increasingly garnered attention of obesity management experts as one of the reasons for selecting treatment options. For example, semaglutide has been shown to reduce fat mass loss by up to 84% in an MRI study in obese population, whereas tirzepatide demonstrated 74% fat mass loss when studied using DXA[3,5]. This is important because it is known that it is the dysfunctional adipose tissue in obesity that leads to various cardiometabolic diseases[6].

Cardiometabolic diseases are in a progressive spectrum and the latest international guidelines recommend that the ultimate treatment goal is to prevent end-organ damage and death[7,8]. Semaglutide has been studied in multiple phase III end-organ trials, and has shown: (1) major adverse cardiovascular events (MACE) reduction, in type 2 diabetes (T2DM) population (SUSTAIN-6, SOUL studies)[9,10] and in an obese population without diabetes (SELECT study)[11], (2) major adverse kidney events (MAKE) reduction in T2DM population (FLOW study)[12]; (3) metabolic dysfunction-associated

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steatohepatitis (MASH) improvement (ESSENCE study)[13]. Tirzepatide, a more recent molecule available in clinical practice, has shown MACE reduction noninferior to dulaglutide in T2DM population (SURPASS-CVOT study)[14], and its cardiovascular benefits in obese population without diabetes is being investigated in the ongoing SURMOUNT-MMO study[15].

As real-world use expands, clinicians increasingly encounter scenarios requiring therapeutic switching[16]. The SURPASS-SWITCH-2 trial studied conversion from semaglutide to tirzepatide in T2DM population but there is no study to show the reverse option[17]. In this area lacking the manufacturer's guidance and clinical protocols, pragmatic guidance to semaglutide switching, grounded in real-world clinical experience becomes valuable.

RATIONALE(S) FOR SWITCHING BETWEEN AGENTS

Switching decisions are multifactorial and individualized. Decision-making in health is described by George Engel in 1977 as dynamic interactions between biomedical, psychological, social factors[18]. These factors stem from various perspectives as shown below in Table 1.

PRAGMATIC DOSE TRANSITION GUIDANCE

Both tirzepatide and semaglutide's weight loss effects are dose-dependent[2-4]. In the absence of formal switching algorithms, the following practical approach can be considered in real-world clinical settings. This decision should be based on patient's tolerability, while taking into account any prior history of treatment with tirzepatide (Table 2).

Table 1. Reasons for Switching Anti-Obesity Medication

Proactive reasons	Reactive reasons
Biomedical factors	
• Clinical need for further efficacy: weight loss	• Adverse experience (e.g., lack of tolerability, lack of efficacy)[19]
• Organ protection (e.g., cardiovascular-, reno-protection, liver health, joint health) or quality of life	• Drug interactions (e.g., with contraception)
• Optimization of barophenotype/ adipose topography; i.e., more fat loss is required	• Need for flexibility in dosing
Psychological factors	
• *Perceived* superiority	• *Perceived* inadequacy of current medication
• Preference for a particular delivery device[20]	
Social factors	
• Encouragement from family, friends, colleagues/peers, influence from media	• Easier availability/ access/affordability

As there is no available evidence that guides dosing for switching (vs. a well-established initiation for naïve patients), we need to have a pragmatic and practical clinical guidance on *how* to switch to semaglutide. For example, the weekly initiation dose of subcutaneous semaglutide is 0.25 mg, but there are no specific recommendations for switching from other incretin-based therapies, such as tirzepatide. The design of the delivery devices of the medications allows for flexible dosing (microdosing)[21].

The treating physician should individualize the respective initiation dose and up-titration schedule. In reality, a flexible titration strategy (known as microdosing) has been a practical option for multiple reasons; to tailor treatment based on achieving clinical efficacy goals while mitigating risk of gastrointestinal adverse events. As there is no formal recommendation from manufacturers, clinicians should be the stewards for this, placing patient safety as first priority while optimizing outcomes according to the individual patient's treatment responses[22].

For example, for a patient transitioning from tirzepatide 5 mg to semaglutide 1.7 mg, for better weight loss efficacy, and to balance clinical efficacy goals with tolerability, physicians may consider a faster transition schedule, adjusted according to patient's clinical response. Escalation interval can be determined when patient tolerates the dose well.

Table 2. Suggested Doses of Semaglutide when Switch from Tirzepatide is Relevant

	Reasons for switch to semaglutide	
	Lack of efficacy	Lack of tolerability
Current tirzepatide dose	Suggested semaglutide dose	Suggested semaglutide dose
2.5 mg	0.5 mg	0.25 mg
5 mg	1 mg	0.5 mg
7.5 mg	1.7-2.4 mg	1 mg
10 mg	2.4 mg	1.7 mg
12.5 mg	2.4-7.2 mg	1.7-2.4 mg
15 mg	2.4-7.2 mg	1.7-2.4 mg

Note: Semaglutide 7.2 mg has been approved by the FDA and EMA (European Medicines Agency) but the dosage of 7.2 mg in a single device may not yet be readily available. Given its recent approval, real-world experience is still limited; caution should be taken and gradual up-titration is recommended[23,24].

CLINICAL CONSIDERATIONS WHEN SWITCHING BETWEEN AGENTS

In real-world practice, switching to semaglutide may not replicate the consistency observed in clinical trials, due to differences in follow-up intensity, pharmacovigilance, and access to behavioral support. Early-phase monitoring during transition is often less structured, which may influence the identification and management of tolerability issues or perceived suboptimal efficacy. In addition, variations in dose-escalation protocols and the delivery of behavioral interventions between trial settings and routine care can affect treatment response. These factors highlight the need for a pragmatic, individualized approach to switching, with attention to counseling, follow-up, and flexible dose titration to optimize outcomes.

CONCLUSION

Switching between glucagon-like peptide-1–based therapies is increasingly common in clinical practice. Although prospective evidence guiding transitions from tirzepatide to semaglutide is lacking, pragmatic real-world approaches can support safe and individualized care. Structured, clinically supervised transitions may enhance continuity of weight management while ensuring safety and cost-effectiveness—ultimately benefiting patients in their long-term obesity treatment journey.

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