One Size Does Not Fit All: Understanding Microdosing Semaglutide for Diabetes in Multidose Pens

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Glucagon-like peptide 1 receptor agonists (GLP-1RA) have transformed the landscape of type 2 diabetes and chronic weight management (1). Clinical trials have shown that GLP-1RA reduce cardiac events in at-risk patients, and indications for other chronic conditions are on the horizon. However, the beneficial clinical outcomes must be weighed against gastrointestinal (GI) side effects, high costs, and shortages that can limit access to use (2). To address these limitations, advocacy for tailored approaches that meet the needs of patients who may benefit from GLP-1RA is imperative.

Dose-limiting tolerability issues and limited supply due to high demand for GLP-1RA have forced clinicians to consider creative approaches for therapeutic continuity (2). Microdosing is an alternative strategy that allows for fractional doses. While unconventional, microdosing offers a tailored solution to maximize therapeutic benefit, minimize adverse effects, and address availability concerns. Semaglutide for diabetes in multidose pens (semaglutide-MDP) is available in multiple strengths and is contained in pen devices that can administer fractional doses of medication (3). Liraglutide is also available in multidose pens, and tirzepatide vials offer another means for GLP-1RA microdosing (4,5). This unique delivery technique may be useful when standard dosing is not ideal.

Microdosing with semaglutide-MDP can be beneficial for patients who experience significant GI adverse effects, which are common with GLP-1RA. Allowing for small, incremental dose adjustments can optimize treatment outcomes by increasing tolerability. Furthermore, microdosing may serve a critical role in clinical scenarios where dose flexibility is needed, such as after hospital discharge or during acute illness. Microdosing allows for dose reductions without requiring a new prescription or refill and is therefore useful in situations where quick, temporary adjustments are necessary.

The surge in demand for GLP-1RA has resulted in intermittent global shortages and gaps in therapy due to variable medication availability. Patients unable to access their usual dose due to shortages or cost barriers have turned to unregulated versions of GLP-1RA, introducing health risks from unverified preparations. Continued use of approved products through microdosing may provide a safer and more consistent alternative, allowing for dose adjustments without significant disruptions in therapy.

The following scenarios should be considered for clinical application of microdosing.

- Transitioning between GLP-1RA. Microdosing can help patients transition to a new GLP-1RA through gradual dose adjustments to improve therapeutic response.
- Dose escalation or de-escalation. Microdosing supports a controlled titration or taper to safely adjust for necessary dose changes.
- Poor tolerability. For patients with severe GI side effects, starting with microdosing and increasing slowly can improve tolerability and prevent therapeutic disruption.
- Cash payers. For patients paying out of pocket, microdosing can extend the use of each pen, reducing costs and improving access when insurance coverage is unavailable.

Both patients and providers should be provided education on microdosing. Each semaglutide-MDP device delivers approximately 72 unnumbered "clicks" of medication. Clinicians should counsel patients to use the pen dosing window to count and administer a specific number of clicks based on individualized dosing (Fig. 1). Clinicians should provide this information through verbal and written instructions and use demonstration devices to ensure patients are comfortable with this dosing technique. The beyond-use date of semaglutide-MDP is 56 days at room temperature or refrigerated; any remaining medication should be discarded after this time according to package labeling (3). Only four to six pen needles are provided with each original package, therefore additional 32G pen needles are recommended to ensure adequate supplies.

In terms of safety and efficacy considerations, while the practical benefits of microdosing are encouraging, this method lacks extensive evidence-based support. Microdosing semaglutide-MDP is considered off-label and is not endorsed by the manufacturer, as no clinical trials have validated its safety or

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Microdosing Instructions for Semaglutide-MDP

Semaglutide-MDP 0.25/0.5 mg	Number of Clicks	Dosing
0.06 mg	9 clicks	Once weekly *** weeks
0.13 mg	18 clicks	Once weekly *** weeks
0.25 mg	36 clicks	Once weekly *** weeks
0.29 mg	42 clicks	Once weekly *** weeks
0.33 mg	48 clicks	Once weekly *** weeks
0.38 mg	54 clicks	Once weekly *** weeks
0.42 mg	60 clicks	Once weekly *** weeks
0.46 mg	66 clicks	Once weekly *** weeks
0.5 mg	72 clicks	Once weekly *** weeks

Semaglutide-MDP 1 mg	Number of Clicks	Dosing
0.13 mg	9 clicks	Once weekly *** weeks
0.25 mg	18 clicks	Once weekly *** weeks
0.5 mg	36 clicks	Once weekly *** weeks
0.58 mg	42 clicks	Once weekly *** weeks
0.67 mg	48 clicks	Once weekly *** weeks
0.75 mg	54 clicks	Once weekly *** weeks
0.83 mg	60 clicks	Once weekly *** weeks
0.92 mg	66 clicks	Once weekly *** weeks
1 mg	72 clicks	Once weekly *** weeks

Semaglutide-MDP 2 mg	Number of Clicks	Dosing
0.25 mg	9 clicks	Once weekly *** weeks
0.5 mg	18 clicks	Once weekly *** weeks
1 mg	36 clicks	Once weekly *** weeks
1.17 mg	42 clicks	Once weekly *** weeks
1.33 mg	48 clicks	Once weekly *** weeks
1.5 mg	54 clicks	Once weekly *** weeks
1.67 mg	60 clicks	Once weekly *** weeks
1.83 mg	66 clicks	Once weekly *** weeks
2 mg	72 clicks	Once weekly *** weeks

Semaglutide-MDP; semaglutide (Ozempic) for diabetes in multidose pens

All doses should be administered subcutaneously once weekly.

Duration of individualized microdoses should be determined at the discretion of prescriber.

Bolded numbers represent standard dosing for Semaglutide-MDP.

Manufacturer recommends discarding in-use pen after 56 days.

Figure 1—Example patient handout for semaglutide-MDP microdosing. This infographic represents a potential handout to be given to people living with diabetes to provide instructions on microdosing via currently available semaglutide-MDP. As possible, microdosing tables and discard instructions should also be provided through the electronic health record using the "SmartPhrases" to ensure ready access to microdosing charts.

efficacy (3). This lack of official guidance necessitates caution and close monitoring to detect adverse effects or inefficacy.

Patient selection is crucial, as microdosing is primarily suited for patients with a certain degree of health literacy, adequate vision, and appropriate dexterity. Candidates for microdosing should demonstrate a clear understanding and the ability to follow complex instructions, as dosing errors could lead to subtherapeutic effects or increased side effects. Patients with a high risk of confusion or cognitive impairment may not be suitable candidates for this strategy.

As the landscape for GLP-1RA continues to evolve, clinicians should consider microdosing as a patient-centered approach to care. With careful patient selection, thorough counseling, and consistent monitoring, microdosing could play a valuable role in optimizing therapy amid challenges in availability, affordability, and tolerability.

In the absence of evidence-based guidance, these recommendations offer an alternative method when navigating known barriers to GLP-1RA use. Clinicians are encouraged to publish their experiences with GLP-1RA microdosing to expand the body of knowledge, provide insights on best practices, and guide others in navigating similar challenges in patient care.

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