Guidelines for Sublingual GLP-1 Tablets

Expected Dissolution Time:

- Dissolution time may vary depending on the individual and the placement of the tablet inside the mouth. Placing the tablet under the tongue is recommended for optimal absorption.
- Tablets are expected to dissolve within approximately 30 seconds to 2 minutes.
- **Instructions:** *Dissolve one tablet under the tongue once daily.*

Timing Around Meals:

- For best absorption, take the tablet on an empty stomach. Avoid food or liquids for at least 30 minutes to 1 hour post-administration. A small amount of water (less than ½ cup) is unlikely to interfere with effectiveness if necessary.

Dose Equivalence When Switching from Injection to Sublingual Tablets:

- There is currently no established dosing equivalence between injectable and sublingual semaglutide. Injectable semaglutide has a bioavailability of around 89%, while oral is approximately 1%, and sublingual is estimated to be similar.
- Dosing adjustments can consider the half-life of semaglutide (5-7 days) and daily administration with sublingual tablets. Our sublingual tablets contain ingredients that support semaglutide absorption, similar to Rybelsus, which is FDA-approved for oral use.
    - The maximum Rybelsus dose (14 mg daily) is considered equivalent to Ozempic 0.5 mg weekly. For patients transitioning from 1 mg injectable and aiming to maintain rather than lose additional weight, sublingual tablets may be a viable option.

Additional Notes on Tirzepatide:

- No oral or sublingual form of tirzepatide is currently available, and there is limited research. However, based on peptide size and patient and prescriber feedback, dosing assumptions have been generally well-tolerated.

Suggested Monthly Titration Dosing Schedules:

Semaglutide

- Month 1: 1 mg daily
- Month 2: 2 mg daily
- Month 3+: 3 mg or 4 mg daily (can use two 2 mg tablets if needed)

Tirzepatide

- Month 1: 3 mg daily
- Month 2: 4 mg daily
- Month 3+: 5 mg daily

Switching Between GLP-1 Medications:

Sublingual Tablets:

- For patients switching between GLP-1 medications in sublingual tablet form, a titration or off-week may not be necessary unless there have been issues tolerating the original medication. If tolerance issues occur, a waiting period of one week may be advisable to ensure the original drug has left the system.
- Maintaining a steady level of GLP-1 in the body is crucial, as the bioavailability of sublingual tablets is relatively low, and off-time may slow progress.
- For the first dose when switching medications, the patient should start with the lowest available dose of the new drug. If the patient is not starting from the lowest dose, a half tablet of the next available dose can be taken to assess tolerance. For example, when switching from semaglutide to tirzepatide, a 3 mg tirzepatide tablet or half of a 4 mg or 5 mg tablet may be used to ensure tolerance.
- Dosage adjustments can be made as tolerated. If patients take a break from GLP-1 tablets for more than a week to a month, prescribers typically restart them at the beginning of the titration schedule.

Injections:

- Prescribers may use several methods when transitioning patients between injectable GLP-1 medications. Some prescribers adopt a conservative approach, gradually titrating the patient from one medication to another, while others may introduce an off-week or switch the patient directly to the new medication on the next scheduled dose.
- Regardless of the current semaglutide dose, starting tirzepatide at the initial 2.5 mg dose once weekly is recommended to observe patient response.
- For patients who titrated down from semaglutide, a gradual titration up of tirzepatide (at a rate of 4 weeks per dose increment) is advisable. However, some prescribers may suggest increasing doses weekly, as tolerated, until reaching the corresponding dose of the previous medication.
- Tirzepatide doses generally increase in increments of 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, and 15 mg. The maximum dose is 15 mg, but many patients may find 10 mg sufficient for their needs and remain at that level.

Additional Notes:

- It is common for prescribers to tailor each transition based on individual patient tolerance and response to the medication, adjusting dosing schedules as needed to minimize side effects and optimize therapeutic outcomes.