

Tirzepatide Terrain Safety & Stability Sheet

Applies to: All LoCITT-T participants (tirzepatide ± concomitant meds)

Purpose: Prevent avoidable destabilization events in multi-system Long COVID and ME/CFS patients by tracking physiologic “terrain readiness.”

A. Core Logic (STAIR + VitalGuard Integration)

Metric	Ideal Range	Alert Threshold	Notes
Heart-Rate Variability (HRV)	>45 ms (RMSSD)	<30 ms	Low HRV = autonomic overload; delay dose 3–5 days if <30 ms.
Resting HR	60–90 bpm	>105 bpm for >2 days	Persistent tachycardia → check dehydration & orthostasis.
Sleep Duration	≥ 6 h/night	< 4 h for 2 consecutive nights	Signal of sympathetic storm; advise pacing.
AQI (PM_{2.5})	0–50	> 100 for > 24 h	High risk for MCAS/asthma flare; use air purifier ≥ HEPA 13.
Humidity	35–50 %	> 65 % or < 25 %	Excess humidity → mold risk; low → airway dryness.
BP Variability (SD / 24 h)	< 12 mmHg	> 20 mmHg	Marker of autonomic instability.
Step Count Trend	Stable ± 10 %	≥ 25 % spike or drop	Indicates overexertion or crash onset.

Terrain Readiness Score (TRS)

$$\text{TRS} = (\text{HRV} \times 0.3) + (\text{Sleep} \times 0.2) + (\text{AQI} \times -0.2) + (\text{Humidity} \times -0.1) + (\text{BP Stability} \times 0.2)$$

- **TRS ≥ 0.7** = Green Zone – safe to dose.
- **0.5–0.69** = Yellow Zone – proceed with monitor check-in.
- **< 0.5** = Red Zone – hold dose and stabilize.

B. Intervention Matrix

Terrain Risk	Recommended Action	Responsible Party
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Low (Green)	Proceed per protocol.	Participant + study nurse.
Moderate (Yellow)	Delay dose 48–72 h, increase electrolytes and rest.	Nurse review call.
High (Red)	Temporary hold tirzepatide, submit flare report, re-score after 24 h.	PI sign-off required.

C. Safety Dependencies

- **MCAS & POTS cohorts:** add antihistamine stack (Ketotifen + H1/H2) and fluid support day before dose.
- **Autoimmune profiles:** monitor CRP / ANA monthly.
- **Mitochondrial exhaustion:** maintain CoQ10 100 mg + B-vitamin support.
- **Hormone-low profiles:** adjust dose timing to luteal phase when possible (female patients).

D. Emergency Protocol

If TRS drops > 0.3 within 48 h post-dose:

1. Hold further doses.
2. Initiate hydration + salt support.
3. Log environmental factors (AQI, mold, temp).
4. Report to safety officer within 12 h.