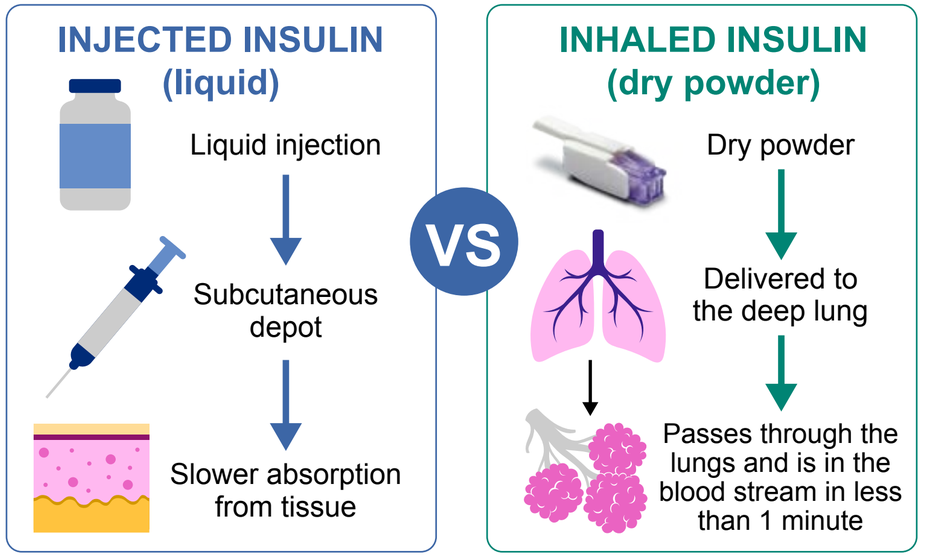
The Inhaled Insulin Dosing Journey

A Practical Guide to Initiation and Optimization



Product and Approved Indication

- Inhaled insulin is a rapid-acting human insulin indicated to improve glycemic control in adult and pediatric patients 6 years of age and older with diabetes mellitus
- Inhaled insulin is administered by oral inhalation using an inhaler at the beginning of each meal
- Patients with T1D must use inhaled insulin with basal insulin



4 inhaled units = 2 injected units (bioequivalent)

TIMING OF INSULIN EFFECT

~ 12 MINUTES
First measurable glucose-lowering effect

~ 35-45 MINUTES
Mean peak effect

~ 90-270 MINUTES
Return to baseline (depending on dose)

Inhaled insulin begins to exert a measurable glucose-lowering effect at ~12 minutes; the time to peak effect and return to baseline increases with dose

1 START

2 TITRATE TO EFFECT

3 CLINICAL EVIDENCE - ADULTS

4 CLINICAL EVIDENCE - PEDIATRICS

References: AFREZZA® (insulin human) [package insert]. Danbury, CT: MannKind Corporation; latest revision May 2026. https://afrezza.com/pdf/full-prescribing-information

Abbreviations: T1D, type 1 diabetes.

Prescribing Information: Consult the full Prescribing information (US PI) for complete and up-to-date information.

1 START | Establish the initial dose

INITIAL DOSE

For insulin-naive patients, initiate treatment with 4 units at the beginning of each meal and titrate to effect



APPROVED CONVERSION TABLE

Current Injected Mealtime Insulin Dose (units)	Starting Inhaled Insulin Dose* (units)	# of cartridges needed: 4 units (blue)	8 units (green)	12 units (yellow)
Up to 3	4 units	1		
4 - 5	8 units		1	
6 - 7	12 units	1 +	1	or / 1
8 +	16 units		1 +	1

*A baseline FEV_1 must be obtained prior to starting inhaled insulin therapy.
For doses ≥16 units, use a combination of 4-, 8-, 12-unit cartridges.

GOAL Start with an appropriate, evidence-based dose to improve safety and tolerability

TRAIN

Train patients and/or caregivers on correct cartridge, inhaler, and administration technique



GOAL Ensure correct technique for optimal delivery and treatment response

Start with the right foundation. Build confidence. Set the stage for success.

A careful start supports safe initiation, effective dosing, and long-term outcomes.

References: AFREZZA® (insulin human) [package insert]. Danbury, CT: MannKind Corporation; latest revision May 2026. https://afrezza.com/pdf/full-prescribing-information

Abbreviations: FEV_1, forced expiratory volume in 1 second.

Prescribing Information: Consult the full Prescribing information (US PI) for complete and up-to-date information.

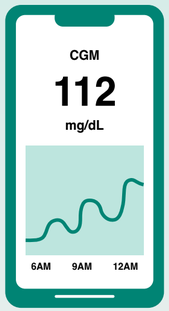
2 TITRATE TO EFFECT

Optimize dosing based on the individual glucose targets

ASSESS EARLY

PREMEAL

Review premeal sensor glucose and determine individualized correction dose



Premeal correction dose example

4 units

IDENTIFY PATTERNS

Use meal plans and repeatable glucose patterns to determine the dose recommendation for the meal

Meal dose recommendation example

8 units

TOTAL DOSE

Add both values to determine the total prandial inhaled dose



Total inhaled dose example

12 units

Use premeal glucose and identify patterns to calculate the total prandial dose

TITRATE WITH PURPOSE

USE AVAILABLE CARTRIDGE STRENGTHS AND COMBINATIONS


4 units


8 units


12 units

EXAMPLES OF COMBINATIONS


= **8** units


= **12** units


= **20** units

SUPPLEMENTAL DOSING (CLINICAL TRIALS)

As soon as 60 minutes after the previous dose, a supplemental dose can be taken [1,2,3]


TAKE THE MEALTIME DOSE


WAIT 60-90 MINUTES


CHECK GLUCOSE

IF ABOVE PROTOCOL-DEFINED THRESHOLD


TAKE SUPPLEMENTAL DOSE

This is a protocol example only. Refer to clinical trial protocols and clinical judgment for guidance on supplemental dosing.

Average inhaled insulin doses per meal across INHALE-1 and INHALE-3.[1,2]


12-20 units

Clinical trials demonstrate the importance of bedtime correction for glycemic management[1,2]



References: AFREZZA® (insulin human) [package insert]. Danbury, CT: MannKind Corporation; latest revision May 2026. https://afrezza.com/pdf/full-prescribing-information 1. Haller et al. Diabetes Care. 2026;49(1):1-9. 2. Hirsch et al. Diabetes Care. 2025;48(3):353-360. 3. Kaiserman et al. J Diabetes Sci Technol. 2024;18(2):397-401.

Abbreviations: N/A

Prescribing Information: Consult the full Prescribing information (US PI) for complete and up-to-date information.

3 CLINICAL EVIDENCE – ADULTS

Across adult studies, inhaled insulin dosing was individualized according to glycemic response

INHALE-3 STUDY PROGRAM

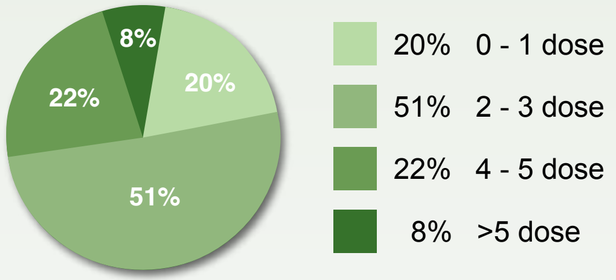
STUDY	POPULATION	INTERVENTION	DURATION
INHALE-3 RCT[1]	123 adults with T1D	Inhaled insulin + degludec vs usual care (AID or MDI)	17 weeks
INHALE-3 EXTENSION[2]	45 adults with T1D	Inhaled insulin + degludec	30 weeks (17 weeks RCT + 13 weeks extension)
INHALE-3 SWITCH[3]	49 adults with T1D	Patients who switched from usual care to inhaled insulin + degludec	13 weeks
INHALE-3 MEAL CHALLENGE[4]	122 adults with T1D (inhaled insulin, n=61; RAA, n=61)	Patients using MDI, nonautomated pump or AID	N/A

DOSING APPROACH

- Initial inhaled insulin dose = Double the RAA dose and round down to the nearest available inhaled insulin dose
- Assess 1-hr PPG during 4- week titration
- Increase the premeal dose by: 4 units when 1-hour PPG was >140mg/dL; 8 units when 1-hour PPG was >200 mg/dL
- Adjust meal dose according to the premeal CGM glucose and meal size
- Correction dosing 60-90 minutes after a prior inhaled insulin dose if needed
- **Bedtime: 4-unit correction if glucose >200 mg/dL**

INHALE-3 STUDY DOSING ANALYSIS[1,2,3,4]

CORRECTION DOSES PER DAY AT WEEK 17[1]



INITIAL PRANDIAL DOSE TO TITRATED PRANDIAL DOSE[2]

Week 1: **36** units → Week 30: **53** units

DAYTIME TIR AFTER 13 WEEKS[3]

70-180 mg/dL

Week 17: **50%** → Week 30: **55%**

+5.1% percentage points mean change from baseline

95% CI: 0.3% to 9.8%
Noninferiority P<0.001
Superiority P=0.04

POSTPRANDIAL GLUCOSE RESPONSE[4]

- PPGE over 2 hours was less with inhaled insulin vs injected RAA (P=0.02)
- Peak glucose was lower with inhaled insulin (P=0.01)
- HbA1c ≤7%: 24% on MDI → 48% after 30 weeks of inhaled insulin

Note: INHALE-3 met its primary endpoint. Selected dosing and clinical findings are shown; complete study results are not presented.

References: 1. Hirsch et al., Diabetes Care. 2025;48(3):353-360. 2. Beck et al. Diabetes Technol Ther. 2025a;27(3):170-178. 3. Beck et al. Diabetes Technol Ther. 2025b;27(3):161-169. 4. Hirsch et al. Diabetes Care. 2024;47(9):1682-1687.

Abbreviations: AID, automatic insulin delivery; CGM, continuous glucose monitoring; CI, confidence interval; MDI, multiple daily injections; PPG, postprandial glucose; PPGE, postprandial glucose excursion; RAA, rapid-acting analog; RCT, randomized controlled trial; TIR, time in range; T1D, type 1 diabetes.

Prescribing Information: Consult the full Prescribing information (US PI) for complete and up-to-date information.

4 CLINICAL EVIDENCE – PEDIATRICS

Supports individualized dosing and titration in pediatric patients

INHALE-1 RCT[1]

STUDY DESIGN:

- 230 pediatric participants, aged 4-17 years, with diabetes
- Inhaled insulin + basal vs injected RAA + basal
- 26 weeks

STARTING APPROACH:

- First inhaled insulin dose = approximately 2 x previous RAA dose
- First dose in clinic with standardized meal
- Glucose response to meal used to establish initial dosing

MEAL AND CORRECTION PROTOCOL:

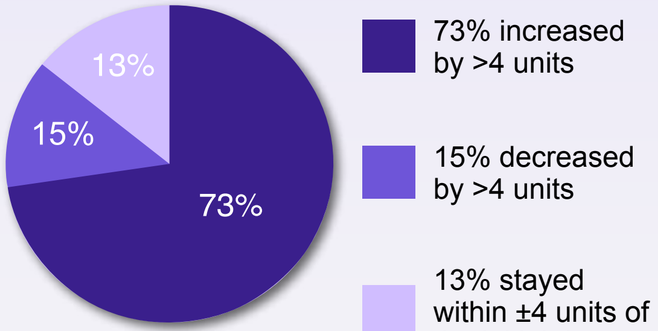
- Meal dose at the start of the meal or no later than 20 minutes after meal initiation
- The study protocol added 4 units when premeal glucose was >160 mg/dL or for a larger-than-usual carbohydrate meal and reduced the dose by 4 units for a smaller-than-usual meal
- A 4-unit correction dose could be administered 60-90 minutes after the prior dose when glucose was >160 mg/dL; bedtime correction dosing was also evaluated

TITRATION APPROACH:

- Adjust meal doses based on glucose response
- Target 60- to 90- minute PPG: 70-160 mg/dL
- Review CGM patterns of hypoglycemia and hyperglycemia to guide dose adjustment
- Week 26: mean daily inhaled insulin dose / baseline RAA dose = 2.96
- The basal/bolus ratio was ~50%/50% on RAA prior to initiating inhaled insulin and 30%/70% after titrating inhaled insulin in the pediatric and adult clinical studies[3]
- Inhaled insulin dose commonly increased beyond initial conversion dose

INHALE-1 RCT DOSING ANALYSIS[2]

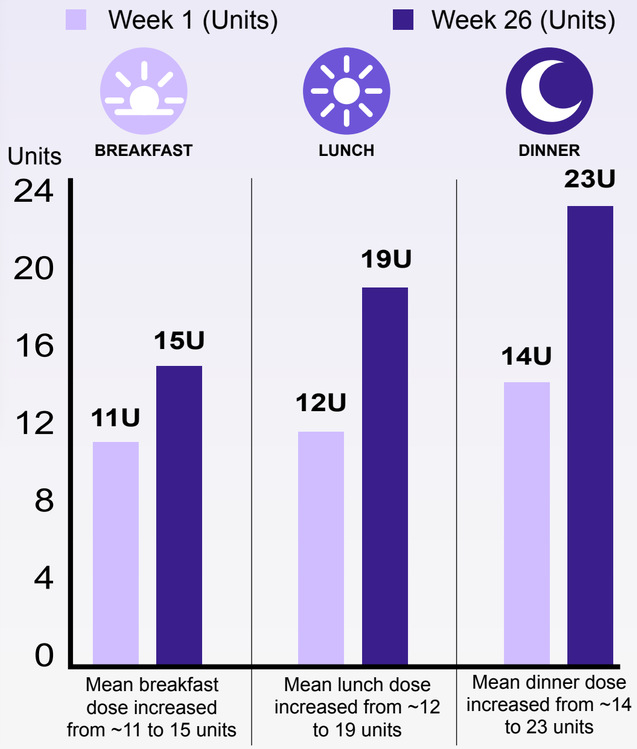
TOTAL DAILY DOSE TITRATION AFTER 26 WEEKS



INITIAL PRANDIAL DOSE TO TITRATED PRANDIAL DOSE

Week 1	Week 26
48 units	72 units

CHANGE IN INHALED INSULIN MEAL DOSE OVER 26 WEEKS



Note: INHALE-1 did not meet its primary endpoint. Selected dosing and clinical findings relevant to this resource are presented; this slide does not represent the complete study results.

References: 1. Haller et al. Diabetes Care. 2026;49(1):1-9. 2. Kaiserman et al. Advanced Technologies & Treatments for Disease. ATTD Poster Presentation. 2026;March 11-14: Barcelona, Spain. 3. Hirsch et al. Diabetes Care. 2024;47(9):1682-1687.

Abbreviations: CGM, continuous glucose monitoring; PPG, postprandial glucose; RAA, rapid-acting analog; U, unit.

Prescribing Information: Consult the full Prescribing information (US PI) for complete and up-to-date information.