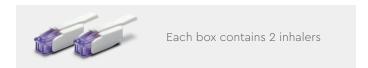


PRODUCT REFERENCE GUIDE

Afrezza® is dispensed in convenient boxes to meet your patients' mealtime insulin needs.¹

See below for a product reference guide, including all Afrezza NDC codes, their contents, and the maximum daily units per box.



	NDC	Afrezza Box Contents	1 Box (30-day supply)	2 Boxes (30-day supply)	3 Boxes (30-day supply)
COMBINATION BOX OPTIONS	NDC 47918-0902-18	Afrezza 4, 8 & 12 Unit Cartridges [60] 4-unit cartridges [60] 8-unit cartridges [60] 12-unit cartridges Total: 180 cartridges	Total Insulin Units: 1440 Total Cartridges: 180 Max Total Daily Dose: 48 units	Total Insulin Units: 2880 Total Cartridges: 360 Max Total Daily Dose: 96 units	Total Insulin Units: 4320 Total Cartridges: 540 Max Total Daily Dose: 144 units
			Example Directions for Use: Inhale 4–16 units by mouth at mealtime and additional units as needed for glucose control. Max total daily dose units.		
	NDC 47918-0880-18	Afrezza 4 & 8 Unit Cartridges [90] 4-unit cartridges [90] 8-unit cartridges Total: 180 cartridges	Total Insulin Units: 1080 Total Cartridges: 180 Max Total Daily Dose: 36 units	Total Insulin Units: 2160 Total Cartridges: 360 Max Total Daily Dose: 72 units	Total Insulin Units: 3240 Total Cartridges: 540 Max Total Daily Dose: 108 units
			Example Directions for Use: Inhale 4–12 units by mouth at mealtime and additional units as needed for glucose control. Max total daily dose units.		
COME		Afrezza 8 & 12 Unit Cartridges [90] 8-unit cartridges [90] 12-unit cartridges Total: 180 cartridges 1800 Afrezza Insulin Units	Total Insulin Units: 1800 Total Cartridges: 180 Max Total Daily Dose: 60 units	Total Insulin Units: 3600 Total Cartridges: 360 Max Total Daily Dose: 120 units	Total Insulin Units: 5400 Total Cartridges: 540 Max Total Daily Dose: 180 units
	NDC 47918-0898-18		Example Directions for Use: Inhale 8–12 units by mouth at mealtime and additional units as needed for glucose control. Max total daily dose units.		
SINGLE BOX OPTIONS	NDC 47918-0874-90	Afrezza 4-Unit Cartridges [90] 4-unit cartridges Total: 90 cartridges 360 Afrezza Insulin Units	Total Insulin Units: 360 Total Cartridges: 90 Max Total Daily Dose: 12 units	Total Insulin Units: 720 Total Cartridges: 180 Max Total Daily Dose: 24 units	Total Insulin Units: 1080 Total Cartridges: 270 Max Total Daily Dose: 36 units
			Example Directions for Use:		
			Inhale 4 units by mouth at mealtime and additional units as needed for glucose control. Max total daily dose units.		
	NDC 47918-0878-90	Afrezza 8-Unit Cartridges [90] 8-unit cartridges Total: 90 cartridges 720 Afrezza Insulin Units	Total Insulin Units: 720 Total Cartridges: 90 Max Total Daily Dose: 24 units	Total Insulin Units: 1440 Total Cartridges: 180 Max Total Daily Dose: 48 units	Total Insulin Units: 2160 Total Cartridges: 270 Max Total Daily Dose: 72 units
			Example Directions for Use:		
			Inhale 8 units by mouth at mealtime and additional units as needed for glucose control. Max total daily dose units.		
	NDC 47918-0891-90	Afrezza 12-Unit Cartridges [90] 12-unit cartridges	Total Insulin Units: 1080 Total Cartridges: 90 Max Total Daily Dose: 36 units	Total Insulin Units: 2160 Total Cartridges: 180 Max Total Daily Dose: 72 units	Total Insulin Units: 3240 Total Cartridges: 270 Max Total Daily Dose: 108 units
		Total: 90 cartridges	Example Directions for Use:		
		1080 Afrezza Insulin Units	Inhale 12 units by mouth at mealtime and additional units as needed for glucose control. Max total daily dose units.		

^{1.} Afrezza (insulin human) Inhalation Powder Prescribing Information. MannKind Corporation.



Indications and Usage:

Afrezza® (insulin human) Inhalation Powder is a rapid acting inhaled human insulin indicated to improve glycemic control in adult patients with diabetes mellitus.

Limitations of Use:

Not recommended for the treatment of diabetic ketoacidosis, not recommended in patients who smoke or have recently stopped smoking.

Important Safety Information

WARNING: RISK OF ACUTE BRONCHOSPASM IN PATIENTS WITH CHRONIC LUNG DISEASE

- Acute bronchospasm has been observed in AFREZZA-treated patients with asthma and COPD
- AFREZZA is contraindicated in patients with chronic lung disease such as asthma or COPD.
- Before initiating AFREZZA, perform a detailed medical history, physical examination, and spirometry (FEV₁) to identify potential lung disease in all patients.

Contraindications

AFREZZA is contraindicated: during episodes of hypoglycemia, in patients with chronic lung disease (such as asthma or chronic obstructive pulmonary disease [COPD]) because of the risk of acute bronchospasm, and in patients with hypersensitivity to regular human insulin or any of the excipients in AFREZZA

Warnings and Precautions

Acute Bronchospasm: In a study of patients with asthma whose bronchodilators were temporarily withheld for assessment, bronchoconstriction and wheezing following AFREZZA dosing was reported. Before initiating therapy, evaluate all patients with a medical history, physical examination, and spirometry (FEV_1) to identify potential underlying lung disease. Do not use in patients with chronic lung disease such as asthma or COPD.

Hypoglycemia or Hyperglycemia with Changes in Insulin Regimen: Glucose monitoring is essential for patients receiving insulin therapy. Changes in insulin strength, manufacturer, type, or method of administration may affect glycemic control and predispose to hypoglycemia or hyperglycemia. These changes should be made under close medical supervision and the frequency of blood glucose monitoring should be increased. For patients with type 2 diabetes, dosage modifications of concomitant oral antidiabetic treatment may be needed.

Hypoglycemia: Hypoglycemia is the most common adverse reaction associated with insulins, including AFREZZA. Severe hypoglycemia can cause seizures, may be life-threatening, or cause death. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery). Hypoglycemia can happen suddenly, and symptoms may differ across patients and change over time in the same patient. Patients and caregivers should be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia.

Decline in Pulmonary Function: AFREZZA causes a decline in lung pulmonary function over time as measured by FEV_1 . In clinical trials excluding patients with chronic lung disease and lasting up to 2 years, AFREZZA-treated patients experienced a small (40 mL) but greater FEV_1 decline than comparator-treated patients. Assess pulmonary function with spirometry at baseline, after the first 6 months of therapy and annually thereafter even in the absence of pulmonary symptoms. In patients who have a decline of \geq 20% in FEV_1 from baseline, consider discontinuing AFREZZA. Consider more frequent lung function assessment in patients with pulmonary symptoms, e.g., wheezing, bronchospasm, breathing difficulties, or persistent or recurring cough. If symptoms persist, discontinue AFREZZA.

Lung Cancer: In clinical trials, 2 cases of lung cancer were observed in patients exposed to AFREZZA while no cases were reported for the comparators. In both cases, a prior history of heavy tobacco use was identified as a risk factor for lung cancer. Two additional cases of lung cancer (squamous cell and lung blastoma) were reported in non-smokers exposed to AFREZZA after the trial completion. These data are insufficient to determine whether AFREZZA has an effect on lung or respiratory tract tumors. In patients with active lung cancer, a prior history of lung cancer, or in patients at risk of lung cancer, consider whether the benefits of AFREZZA use outweigh this potential risk.

Diabetic Ketoacidosis (DKA): In clinical trials enrolling patients with type 1 diabetes, diabetic ketoacidosis (DKA) was more common in AFREZZA-treated patients (0.43%; n=13) than in comparator-treated patients (0.14%; n=3). Patients with type 1 diabetes should always use AFREZZA in combination with basal insulin. In patients at risk for DKA, such as those with an acute illness or infection, increase the frequency of glucose monitoring and consider discontinuing AFREZZA and giving insulin using an alternate route of administration.

Hypersensitivity Reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including AFREZZA. If hypersensitivity reactions occur, discontinue AFREZZA, treat per standard of care and monitor until symptoms and signs resolve.

Hypokalemia: All insulin products, including AFREZZA, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death. Closely monitor potassium levels in patients at risk of hypokalemia and treat if indicated.

Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs): Fluid retention, which may lead to or exacerbate heart failure, can occur with concomitant use of TZDs and insulin. Observe these patients for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of the TZD should be considered.

Drug Interactions

Certain drugs may affect glucose metabolism, increasing the risk of hypoglycemia or deceasing or increasing the blood glucose lowering effect of AFREZZA. Dose adjustment and increased frequency of blood glucose monitoring may be required. Co-administration of beta-blockers, clonidine, guanethidine, and reserpine with AFREZZA may reduce the signs and symptoms of hypoglycemia. For full list, see Prescribing Information.

Adverse Reactions

The most common adverse reactions associated with AFREZZA are hypoglycemia, cough, and throat pain or irritation. To report SUSPECTED ADVERSE REACTIONS, contact MannKind Corporation at 1-877-323-8505 or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088 (1-800-332-1088).

<u>Full Prescribing Information</u> and <u>Medication Guide</u> for Afrezza, including BOXED WARNING, is available at <u>www.afrezza.com/safety.</u>

