BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.30.028

Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	January 1, 2015
Subject:	Afrezza	**Page:**	1 of 5

Last Review Date: March 6, 2026

Afrezza

Description

Afrezza (insulin human)

Background
Afrezza (insulin human) Inhalation Powder is a rapid-acting inhaled insulin indicated to improve glycemic control in adults with diabetes mellitus. Afrezza is a rapid-acting inhaled insulin that is administered at the beginning of each meal. Afrezza is not a substitute for long-acting insulin. Afrezza must be used in combination with long-acting insulin in patients with type 1 diabetes (1).

Regulatory status
FDA-approved indication: Afrezza is a rapid-acting inhaled insulin indicated to improve glycemic control in adult patients with diabetes mellitus (1).

Limitations of Use (1):

- In patients with type 1 diabetes, must use with a long-acting insulin.
- Not recommended for the treatment of diabetic ketoacidosis.
- Not recommended in patients who smoke.

Afrezza carries a boxed warning regarding the risk of acute bronchospasm in patients with chronic lung disease. Afrezza is contraindicated in patients with chronic lung disease such as asthma or chronic obstructive pulmonary disease (COPD). Before initiating therapy with Afrezza, evaluate all patients with a detailed medical history, physical examination, and spirometry (FEV_1) to identify potential lung disease. Spirometry (FEV_1) should also be assessed after the first 6 months of therapy, and annually thereafter, even in the absence of pulmonary

symptoms. In patients who have a decline of ≥ 20% in FEV_1 from baseline, consider discontinuing Afrezza (1).

The use of Afrezza during episodes of hypoglycemia is contraindicated. Hypoglycemia is the most common adverse reaction associated with insulin, including Afrezza (1).

Safety and effectiveness in pediatric patients have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Afrezza may be considered **medically necessary** if the conditions indicated below are met.

Afrezza may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Diabetes mellitus Type 1
    a. Inadequate treatment response, intolerance, or contraindication to one rapid- or short-acting subcutaneous insulin product
    b. Must be used in combination with long-acting insulin therapy
    c. **NOT** used in combination with an insulin pump

2. Diabetes mellitus Type 2
    a. Inadequate treatment response, intolerance, or contraindication to an oral anti-diabetic agent **AND** long-acting insulin therapy

AND ALL of the following: :

1. Spirometry testing before initiating, after 6 months of therapy, and annually.
2. FEV1 ≥ 70% of predicted value
3. Patient has quit smoking or is in a smoking cessation program
4. **NO** history of chronic lung disease, such as asthma or COPD
5. **NOT** used for the treatment of diabetic ketoacidosis
6. No active lung cancer

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Diabetes mellitus Type 1
    a. Must be used in combination with long-acting insulin therapy
    b. **NOT** used in combination with an insulin pump

2. Diabetes mellitus Type 2

AND the following:

1. Spirometry testing conducted annually

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary
Afrezza is a rapid-acting inhaled insulin indicated to improve glycemic control in adult patients with diabetes mellitus. Afrezza carries a boxed warning for risk of acute bronchospasm in patients with chronic lung disease. Prior to initiating therapy, there should be a complete medical review to identify potential lung disease. Pulmonary function tests should be administered before initiating, after 6 months of therapy, and annually, even in the absence of pulmonary symptoms. Use of Afrezza is contraindicated during hypoglycemic episodes and in patients who have had hypersensitivity reactions to Afrezza or any of its excipients. The safety and efficacy of Afrezza in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Afrezza while maintaining optimal therapeutic outcomes.

References
1. Afrezza [package insert]. Danbury, CT: MannKind Corporation; February 2023.

Policy History

Date	Action
December 2014	Addition to PA
March 2015	Annual editorial review and reference update
September 2016	Annual editorial review and reference update Policy number change from 5.07.16 to 5.30.28
July 2017	Annual review
December 2017	Annual review and reference update
November 2018	Annual editorial review and reference update
December 2019	Annual review and reference update
March 2020	Addition of requirement that patients with Type 1 diabetes do not use in combination with an insulin pump. Also removed the word “basal” when referring to long-acting insulin
June 2020	Annual review
March 2021	Annual editorial review and reference update
December 2021	Annual review
March 2022	Annual review
December 2022	Annual review. Changed policy number to 5.30.028

March 2023	Annual review
March 2024	Annual editorial review and reference update. Revised FEV1 value to ≥70% of predicted value. Per SME, added to initiation requirement for Type 2 DM to t/f long-acting insulin
September 2024	Annual review
March 2025	Annual review
March 2026	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2025.