BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

**PHARMACY COVERAGE GUIDELINE**

# AFREZZA® (insulin human)
# Generic Equivalent (if available)

**This Pharmacy Coverage Guideline (PCG):**
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

**Scope**
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

**Instructions & Guidance**
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

## Medical Necessity Requirements for AFREZZA (insulin human)

## Criteria for Initial Therapy:

### Indication
- Inadequately controlled type 1 diabetes mellitus
  - Must be concurrently on a long-acting insulin product or insulin pump product which will be continued
- Inadequately controlled type 2 diabetes mellitus
  - Must be concurrently on metformin and at least one other oral agent for diabetes mellitus

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## Age Requirement
- 18 years or older

## Baseline Clinical Evaluation
- Unable to self-inject Humalog (insulin lispro), rapid acting insulin, due to **ONE** of the following:
  - Physical impairment
  - Visual impairment
  - Lipohypertrophy
  - Needle phobia as defined by DSM-V criteria for specific phobia
- Hemoglobin A1C is greater than 7%
- Baseline spirometry (FEV1) is greater than 70% of expected normal (repeat spirometry must be done annually to identify potential lung disease)

## Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

## Safety
- No use during hypoglycemia
- No chronic lung disease such as asthma or chronic obstructive pulmonary disease
- No hypersensitivity to regular insulin or any excipients found in Afrezza product
- No active lung cancer
- Does not smoke or has quit smoking greater than six months ago or is using smoke cessation products (e.g., Chantix, Nicorette)
- Will not be used in the treatment of diabetic ketoacidosis

## Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (Hemoglobin A1C, spirometry)
  - Supporting clinical documentation

## Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

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# Criteria for Continuation of Therapy (renewal therapy)
**Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy**

## Clinical Response
- Achieved and maintains at least 20% improvement in Hemoglobin A1C from baseline

- Repeat pulmonary function tests show no decline in FEV1

### Adherence
- Adherence to the prescribed therapy regimen has been documented

### Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

### Safety
- No active lung cancer
- Does not smoke or is using smoke cessation products (e.g., Chantix, Nicorette)
- No new contraindications or significant adverse drug effects such as:
  - Frequent severe bronchospasm, wheezing, breathing difficulties, or persistent or recurring cough
  - Declining pulmonary function defined as a decline of greater than or equal to 20% in FEV1 from baseline
  - Use during hypoglycemia
  - Chronic lung disease such as asthma or chronic obstructive pulmonary disease
  - Hypersensitivity to regular insulin or any excipients found in Afrezza product

### Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use (Hemoglobin A1C, spirometry FEV1)

### Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

## Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

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## Description:

Afrezza (insulin human) inhalation powder is a rapid acting inhaled insulin indicated to improve glycemic control in adult individuals with type 1 or type 2 diabetes mellitus (DM1 or DM2). When used in the treatment of DM1, it must be used with a long-acting insulin. Afrezza (insulin human) inhalation powder is not indicated for use in the treatment of diabetic ketoacidosis, and it is not recommended in individuals who smoke or recently stopped smoking within the last 6 months.

Insulin lowers blood glucose levels by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin also inhibits lipolysis in adipocytes, inhibits proteolysis, and enhances protein synthesis.

For individuals with DM1, an insulin regimen consisting of a basal insulin with insulin administered around meals is the standard of care. For individuals with DM2, lifestyle and behavioral changes with use of metformin are considered as first line therapy. If glycemic control remains inadequately controlled, other oral agents may be added, or insulin can be considered.

Afrezza (insulin human) inhalation powder is available as 4-unit, 8-unit and 12-unit single-use cartridges. The cartridges must be used with the Afrezza breath powered inhaler. The amount of Afrezza (insulin human) inhalation powder delivered to the lung will depend on individual patient factors. The inhaler is used for up to 15 days from the date of first use after which it must be discarded and replaced with a new inhaler. The package label for Afrezza (insulin human) inhalation powder states that the faster absorption from Afrezza (insulin human) inhalation powder did not result in a faster onset of activity when compared to insulin lispro.

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## Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

**Specific phobia: DSM-5 300.29 (ICD-10- F 40.23, F40.231, F40.298)**
***Based on criteria from the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013)***

1. A persistent fear that is excessive or unreasonable, that occurs by the presence or anticipation of a specific object or situation (e.g., flying, heights, animals, receiving an injection, seeing blood).

2. Exposure to the feared item or situation almost always leads to an immediate anxiety response, which may take the form of a panic attack. In children, the anxiety may be expressed by crying, tantrums, freezing, or clinging.

3. The person recognizes that the fear is excessive or out of proportion to the actual threat posed. In children, this feature may be absent.

4. The phobic situation(s) is avoided or else is endured with intense anxiety or distress.

5. The avoidance, anxious anticipation, or distress during the feared situation(s) interferes significantly with the person's normal routine, work (or school) functioning, social activities, relationships, or there is marked distress about having the phobia.

6. The fear is persistent, typically lasting for at least six months.

7. The anxiety, panic attacks, or avoidance associated with the specific object or situation are not better accounted for by another mental disorder, such as Obsessive-Compulsive Disorder, Posttraumatic Stress Disorder, Separation Anxiety Disorder (e.g., avoidance of school), Social Phobia, Panic Disorder, etc.

**Needle phobia:**

A specific phobia characterized by a deep and persistent fear of needles, resulting in symptoms of anxiety. Symptoms may also arise from anticipating the presence of the needles. An individual displaying symptoms of anxiety may be experience:

- Increased heart rate (palpitations)
- Dizziness or unsteadiness
- Nausea
- Sweating
- Shaking or trembling
- An upset stomach
- Breathlessness

Someone suffering from a specific disorder will also display avoidance behavior, meaning that they take steps to avoid having to confront the object or situation at the center of their disorder

**Insulin products:**

**Rapid acting:**
Afrezza (insulin human) – inhaled
Apidra (insulin glulisine human analog)
Humalog (insulin lispro human analog)
Novolog (insulin aspart human analog)

**Short acting:**
Humulin R (insulin human regular)
Novolin R (insulin human regular)

**Intermediate acting:**
Humulin N (insulin human isophane NPH)
Novolin N (insulin human isophane NPH)

**Long acting:**
Basaglar (insulin glargine human analog)
Lantus (insulin glargine human analog)
Levemir (insulin detemir human analog)
Tresiba (insulin degludec human analog)

**Concentrated:**
Humulin R U-500 (insulin human regular)
Toujeo (insulin glargine human analog, U-300)

**Pre-mixed:**
Humalog Mix 50/50 (lispro protamine/lispro)
Humalog Mix 75/25 (lispro protamine/lispro)

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Humulin Mix 70/30 (NPH/regular)
Novolin Mix 70/30 (NPH/regular)
Novolog Mix 70/30 (aspart protamine/aspart)
Ryzodeg 70/30 (degludec/aspart)

**Insulin combinations:**

Soliqua (glargine/lixisenatide)
Xultophy (degludec/liraglutide)

## Resources:

Afrezza (insulin human) oral inhalation powder product information, revised by Mannkind Corporation 02-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 17, 2025.