BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
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AFREZZA® (insulin human)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

AFREZZA® (insulin human)

Criteria:

- **Criteria for initial therapy:** Afrezza (insulin regular, human) inhalation powder is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 18 years of age or older
  2. Hemoglobin A1C is greater than 7%
  3. **ONE of the following:**
     a. **For a confirmed diagnosis of inadequately controlled type 1 diabetes mellitus**, individual is concurrently on a long acting insulin product or insulin pump product which will be continued
     b. **For a confirmed diagnosis of inadequately controlled type 2 diabetes mellitus**, individual is concurrently on metformin and at least 1 other oral agent for diabetes mellitus
  4. Medical record documentation that the individual is unable to self-inject Humalog (insulin lispro), rapid acting insulin, due to **ONE** of the following:
     a. Physical impairment
     b. Visual impairment
     c. Lipohypertrophy
     d. Needle phobia as defined by DSM-V criteria for specific phobia (see Definitions section)
  5. Baseline spirometry (FEV1) is $\geq$ 70% of expected normal, repeat spirometry to be done annually thereafter
  6. The individual does not have active lung cancer
  7. The individual does not smoke or has not recently quit smoking (within the last 6 months)
  8. Will not be used in the treatment of diabetic ketoacidosis
  9. There are **NO** contraindications:
     a. Contraindications include:
        i. Use during hypoglycemia
        ii. Chronic lung disease such as asthma or chronic obstructive pulmonary disease
        iii. Hypersensitivity to regular insulin or any excipients found in Afrezza product

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Afrezza (insulin regular, human) inhalation powder is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. The individual has achieved and maintains at least 20% improvement in HgA1c from the baseline

2. The condition has worsened while on therapy
    a. Worsening is defined as:
        i. Hemoglobin A1c increased while on therapy
        ii. Repeat pulmonary function tests show a decline of 20% or more in FEV1

3. Individual has been adherent with the medication

4. The individual does not have active lung cancer

5. The individual does not smoke

6. Individual has not developed any contraindications or significant adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Frequent severe bronchospasm, wheezing, breathing difficulties, or persistent or recurring cough
        ii. Declining pulmonary function (i.e., spirometry) defined as a decline of greater than or equal to 20% in FEV1 from baseline
        iii. Development of lung cancer

7. There are no significant interacting drugs

Renewal duration: 12 months

- 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 a Non-Cancer Medications**

    2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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.

AFREZZA® (insulin human)

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.

Definitions:

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)
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) inhalation powder product information, revised by Mannkind Corporation 02-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on March 23, 2021.