BlueCross BlueShield of Alabama

Afrezza®
Prior Authorization with Quantity Limit
Criteria Program Summary

This prior authorization applies to Commercial and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Afrezza prior authorization with quantity limit is to encourage appropriate use and the use of cost-effective preferred rapid acting insulin product(s). The program defines appropriate use of Afrezza as requiring patients to have a diagnosis of diabetes mellitus type 1 who are on concomitant long acting insulin therapy or diagnosis of diabetes mellitus type 2; who has received a detailed medical history, physical examination, and spirometry with Forced Expiratory Volume in 1 second (FEV1) to identify potential lung disease; who have not smoked in the past 6 months; and who do not have contraindications to Afrezza. The program also requires the patient to have a documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred rapid acting insulin product(s) that is not expected to occur with the requested product(s). The program will also accommodate for those with a diagnosed needle phobia and for those with a physical or mental disability that will prevent the patient from using the preferred rapid acting insulin product(s). The program will also support a quantity limit of 10,080 units of insulin every 30 days. Requests for Afrezza will be reviewed when patient-specific documentation is provided.

PRIOR AUTHORIZATION AND QUANTITY LIMIT TARGET AGENTS

Afrezza® (regular human insulin inhaled)

PROGRAM PRIOR AUTHORIZATION AND QUANTITY LIMITS

Brand (generic)	GPI	Multisource Code	Quantity Limit
Afrezza (human insulin, inhaled)			
4 units cartridge packs	27104010002940	M, N, O, Y	2,520 cartridges / 30 days
8 unit cartridge packs	27104010002950	M, N, O, Y	1,260 cartridges / 30 days
12 unit cartridge packs	27104010002955	M, N, O, Y	900 cartridges / 30 days
30 x 4 unit cartridge + 60 x 8 unit cartridge mix packs	27104010002970	M, N, O, Y	1,530 cartridges / 30 days
60 x 4 unit cartridge + 30 x 8 unit cartridge mix packs	27104010002975	M, N, O, Y	1,890 cartridges / 30 days
60 x 8 unit cartridge + 30 x 12 unit cartridge mix packs	27104010002986	M, N, O, Y	1,080 cartridges / 30 days
90 x 4 unit cartridge + 90 x 8 unit cartridge mix packs	27104010002978	M, N, O, Y	1,800 cartridges / 30 days
60 x 4 unit cartridge + 60 x 8 unit cartridge + 60 x 12 unit cartridge mix packs	27104010002990	M, N, O, Y	1,260 cartridges / 30 days

PRIOR AUTHORIZATION AND QUANTITY LIMIT CRITERIA FOR APPROVAL

Afrezza will be approved when ALL of the following are met:

1. The patient has ONE of the following diagnoses:
    a. The patient has a diagnosis of diabetes mellitus type 1 AND the patient is on concurrent long acting insulin therapy in the past 90 days
    OR
    b. The patient has a diagnosis of diabetes mellitus type 2

    AND
2. The patient has received ALL of the following to identify any potential lung disease:
    a. Detailed medical history review
    AND
    b. Physical examination
    AND
    c. Spirometry with Forced Expiratory Volume in 1 second (FEV1)

    AND
3. The patient has not smoked in the past 6 months
    AND
4. The patient does not have any FDA labeled contraindication(s) to Afrezza
    AND
5. ONE of the following:
    a. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred rapid acting insulin product(s) that is not expected to occur with the requested product
    OR
    b. The prescriber has documented that the patient has a physical or a mental disability that would prevent him/her from using a preferred rapid acting insulin product(s)
    OR
    c. The patient has a documented needle phobia diagnosis

    AND
6. ONE of the following:
    a. The quantity requested is less than or equal to the program quantity limit
    OR
    b. The quantity (dose) requested is greater than the program quantity limit and the prescriber has submitted documentation in support of therapy with a higher dose/ quantity for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

Length of Approval: 12 months

FDA LABELED INDICATIONS[1]

Insulin Product	Indication	Dosage and Administration	Limitation of Use
Afrezza® (regular human insulin, inhaled)	Rapid acting insulin indicated to improve glycemic control in adult patients with diabetes mellitus.	Administer using a single inhalation per cartridge. Administer at the beginning of a meal. Dosing must be individualized. Before initiating, perform a detailed medical history, physical examination, and spirometry with Forced Expiratory Volume in 1 second (FEV1) in all patients to identify potential lung disease.	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 or who have recently stopped smoking.

CLINICAL RATIONALE

The American Diabetes Association (ADA) Standards in diabetes mellitus recommend the following therapy for type 1 diabetes mellitus: [3]

- Use of multiple-dose insulin injections (3-4 injections per day of basal and prandial insulin) or continuous subcutaneous insulin infusion (CSII) therapy
- Matching prandial insulin to carbohydrate intake, pre-meal blood glucose, and anticipated activity
- Most patients should use insulin analogs to reduce hypoglycemic risk
- Individuals who have been successfully using continuous subcutaneous insulin infusion should have continued access after they turn 65 years of age.[14]

For type 2 diabetes mellitus, the American Diabetes Association recommends the following:

- Metformin, if not contraindicated and if tolerated, is the preferred initial pharmacological agent for type 2 diabetes
- Consider initiating insulin therapy (with or without additional agents) in patients with newly diagnosed type 2 diabetes and markedly symptomatic and/or elevated blood glucose levels or A1C
- If noninsulin monotherapy at maximum tolerated dose does not achieve or maintain the A1C target over 3 months, then add a second oral agent, a glucagon-like peptide 1 receptor agonist, or basal insulin
- A patient-centered approach should be used to guide the choice of pharmacological agents. Considerations include efficacy, cost, potential side effects, weight, comorbidities, hypoglycemia risk, and patient preferences.
- For patients with type 2 diabetes who are not achieving glycemic goals, insulin therapy should not be delayed

The ADA states that inhaled rapid-acting insulin used before meals in type 1 diabetes leads to inferior A1C lowering when compared with aspart insulin, with less hypoglycemia across all A1C target categories.[3]

The AACE/ACE algorithm recommends insulin for T2DM when noninsulin antihyperglycemic therapy fails to achieve target glycemic control or when a patient has symptomatic hyperglycemia. Therapy with long-acting basal insulin is preferred. If glycemic control is not achieved with basal insulin, prandial insulin can be added. Preference should be given to rapid-acting insulins (the analogs lispro, aspart, and glulisine or inhaled insulin) over regular human insulin because the former have a more rapid onset and offset of acting and are associated with

less hypoglycemia. For the treatment of T1DM, regimens that provide both basal and prandial insulin should be used.[2]

Efficacy[1]
Afrezza was studied in adults with type 1 diabetes in combination with basal insulin. The efficacy of Afrezza in type 1 diabetes patients was compared to insulin aspart in combination with basal insulin. Afrezza has been studied in adults with type 2 diabetes in combination with oral antidiabetic drugs. The efficacy of Afrezza in type 2 diabetes patients was compared to placebo inhalation. The efficacy of Afrezza has not been studied in smokers.

Safety[1]
Contraindications to Afrezza include:
- Use during episodes of hypoglycemia
- Chronic lung disease, such as asthma, or chronic obstructive pulmonary disease
- Hypersensitivity to regular insulin or any of the inhaled regular human insulin excipients.

Afrezza contains the following black box warnings:
- Acute bronchospasm has been observed in patients with asthma and COPD using Afrezza
- 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.

The most common adverse reactions associated with Afrezza (2% or greater incidence) are hypoglycemia, cough, and throat pain or irritation.

Acute bronchospasm has been observed following Afrezza dosing in patients with asthma and patients with COPD. In a study of patients with asthma, bronchoconstriction and wheezing following Afrezza dosing was reported in 29% (5 out of 17) and 0% (0 out of 13) of patients with and without a diagnosis of asthma, respectively. In this study, a mean decline in FEV1 of 400 mL was observed 15 minutes after a single dose in patients with asthma. In a study of patients with COPD (n=8), a mean decline in FEV1 of 200 mL was observed 18 minutes after a single dose of Afrezza. The long-term safety and efficacy of AFREZZA in patients with chronic lung disease has not been established.

Afrezza causes a decline in lung function over time as measured by FEV1. In clinical trials excluding patients with chronic lung disease and lasting up to 2 years, Afrezza treated patients experienced a small [40 mL (95% CI: -80, -1)] but greater FEV1 decline than comparator-treated patients. The FEV1 decline was noted within the first 3 months, and persisted for the entire duration of therapy (up to 2 years of observation). In this population, the annual rate of FEV1 decline did not appear to worsen with increased duration of use. The effects of Afrezza on pulmonary function for treatment duration longer than 2 years has not been established. There are insufficient data in long term studies to draw conclusions regarding reversal of the effect on FEV1 after discontinuation of Afrezza. The observed changes in FEV1 were similar in patients with type 1 and type 2 diabetes. Assess pulmonary function (e.g., 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 ≥ 20% in FEV1 from baseline, consider discontinuing Afrezza. Consider more frequent monitoring of pulmonary function in patients with pulmonary symptoms such as wheezing, bronchospasm, breathing difficulties, or persistent or recurring cough. If symptoms persist, discontinue Afrezza.

References:

1. Afrezza prescribing information. Mannkind Corporation. August 2016.
2. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the

comprehensive type 2 diabetes management algorithm. *Endocrine Practice.* Vol 22 No. 1 January 2016.
3. American Diabetes Association. Standards of medical care in diabetes-2016. *Journal of Clinical and Applied Research and Education; 29 (Supp 1): S1-S112.*