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Afrezza (regular human insulin, inhaled) Prior Authorization with Quantity Limit Program Summary

FDA LABELED INDICATIONS AND DOSAGE[1]

Agent(s)	Indication(s)	Dosage
Afrezza® (regular human insulin, inhaled) Inhaled powder	To improve glycemic control in adult patients with diabetes mellitus. Limitations of use: • 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 or who have recently stopped smoking	Administer at the beginning of a meal. Dosing must be individualized. Start insulin naïve patients on 4 units at each meal. See prescribing information for converting injectable insulin patients

CLINICAL RATIONALE

Overview

The American Diabetes Association (ADA) Standards in diabetes mellitus recommend the following therapy for type 1 diabetes mellitus:[2]

- Most people with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or continuous subcutaneous insulin infusion.
- Most individuals with type 1 diabetes should use rapid-acting insulin analogs to reduce hyperglycemia risk.
- Patients with type 1 diabetes should be trained to match prandial insulin doses to carbohydrate intake, premeal blood glucose, and anticipated physical activity.

For type 2 diabetes mellitus (T2DM), the American Diabetes Association recommends the following:[2]

- Metformin is the preferred initial pharmacological agent for the treatment of type 2 diabetes.
- The early introduction of insulin should be considered if there is evidence of ongoing catabolism, if symptoms of hyperglycemia are present, or when A1C levels (greater than 10% (86mmol/mol)) or blood glucose levels (greater or equal to 300 mg/dL (16.7mmol/L)) are very high
- Consider initiating dual therapy in patients with newly diagnosed type 2 diabetes who have A1C levels 1.5-2.0% above their glycemic target.
- A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include comorbidities (atherosclerotic cardiovascular disease, heart failure, chronic kidney disease), hypoglycemia risk, impact on weight, cost, risk for side effects, and patient preferences.
- In most patients who need the greater glucose-lowering effect of an injectable medication, glucagon-like peptide 1 receptor agonists are preferred to insulin. An oral GLP-1 agent is now available.

It has been shown that inhaled rapid-acting insulin used before meals in type 1 diabetes was shown to be noninferior for A1C lowering when compared with aspart insulin, with less hypoglycemia observed with inhaled insulin therapy. There was, however, a greater mean reduction in A1C with insulin aspart than with inhaled insulin (20.21% with inhaled vs. 20.40% with aspart, satisfying the noninferiority margin of 0.4%), and more patients in the insulin aspart group achieved A1C goals of ≤7.0% and ≤6.5%.[3] A pilot study found evidence that compared with injectable rapid-acting insulin, supplemental doses of inhaled insulin taken based on post-prandial glucose levels may improve blood glucose management without additional hypoglycemia or weight gain, although results from a larger study are needed for confirmation.[4]

The AACE/ACE states that patients taking 2 oral antihyperglycemic agents who have an A1C >8.0% and/or long standing T2DM are less likely to reach their target A1C with a third oral antihyperglycemic agent. Although adding a GLP1 receptor agonist as the third agent may successfully lower glycemia, eventually many patients will still require insulin. When insulin becomes necessary, a single daily dose of basal insulin should be added to the regimen. Patients whose glycemia remains uncontrolled while receiving basal insulin in combination with oral agents or GLP1 receptor agonists may require mealtime insulin to cover postprandial hyperglycemia. Rapid-acting injectable insulin analogs (lispro, glulisine, aspart, or fast-acting aspart) or inhaled insulin are preferred over regular human insulin because the former have a more rapid onset and offset of action and are associated with less hypoglycemia.[5] For the treatment of T1DM, regimens that provide both basal and prandial insulin should be used for most patients.[6]

Efficacy
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 in patients who smoke has not been established.[1]

Safety
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 concerning patients with chronic lung disease:
- 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.

References:

1. Afrezza prescribing information. Mannkind Corporation. February 2020.
2. American Diabetes Association. Standards of Medical Care in Diabetes-2021. *Diabetes Care* 2021;44(Suppl. 1):S1-232. https://care.diabetesjournals.org/content/diacare/suppl/2020/12/09/44.Supplement_1.DC1/DC_44_S1_final_copyright_stamped.pdf Accessed 8/28/20.Accessed 10/1/2021
3. Bode BW, McGill JB, Lorber DL, et al. Inhaled Technosphere Insulin Compared With Injected Prandial Insulin in Type 1 Diabetes: A Randomized 24-Week Trial. *Diabetes Care* 2015;38:2266-2273. https://care.diabetesjournals.org/content/38/12/2266.full-text.pdf Accessed 10/1/202021.
4. Akturk HK, Snell-Bergeon JK, Rewers A, et al. Improved Postprandial Glucose with Inhaled Technosphere Insulin Compared with Insulin Aspart in Patients with Type 1

Diabetes on Multiple Daily Injections: The STAT Study. *Diabetes Technol Ther* 2018 Oct;20(10):639-647. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6161328/ Accessed 10/1/2021.
5. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm—2020 Executive Summary. *Endocr Pract.* 2020 Jan;26(1):107-139. Available at: https://www.endocrinepractice.org/article/S1530-891X(20)35066-7/fulltext Accessed 10/1/2021.
6. American Association of Clinical Endocrinologists (AACE) Disease State Resources: Treatment of Type 1 Diabetes. https://pro.aace.com/disease-state-resources/diabetes/depth-information/treatment-type-1-diabetes Accessed 10/1/2021.

Afrezza (regular human insulin, inhaled) Prior Authorization with Quantity Limit

TARGET AGENT(S)
Afrezza® (regular human insulin inhaled)

Brand (generic)	GPI	Multisource Code	Quantity Limit
Afrezza (human insulin, inhaled)			
90 x 4 unit cartridge packs	27104010002940	M, N, O, Y	2,520 cartridges / 30 days
90 x 8 unit cartridge packs	27104010002950	M, N, O, Y	1,260 cartridges / 30 days
90 x 12 unit cartridge packs	27104010002955	M, N, O, Y	900 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
90 x 8 unit cartridge + 90 x 12 unit cartridge	27104010002988	M, N, O, Y	1,080 cartridges / 30 days

PRIOR AUTHORIZATION AND QUANTITY LIMIT CRITERIA FOR APPROVAL
Initial Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
    a. The patient has a diagnosis of diabetes mellitus type 1 AND the patient is currently on long acting insulin therapy
    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. ONE of the following:
    a. The patient's age is within FDA labeling for the requested indication for the requested agent
    OR
    b. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication

    AND
5. ONE of the following:
    a. The patient has an intolerance or hypersensitivity to a preferred rapid acting insulin agent that is not expected to occur with the requested agent
    OR
    b. The patient has an FDA labeled contraindication to a preferred rapid acting insulin agent
    OR

c. The prescriber has provided information 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
d. The patient has a documented needle phobia

AND

6. The patient does not have any FDA labeled contraindications to the requested agent
AND
7. ONE of the following:
    a. The requested quantity (dose) does NOT exceed the program quantity limit
    OR
    b. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose
        AND
        iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: 12 months

Renewal Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process
AND
2. The patient has had clinical benefit with the requested agent
AND
3. 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

4. The patient has not smoked in the past 6 months
AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
6. ONE of the following:
    a. The requested quantity (dose) does NOT exceed the program quantity limit
    OR
    b. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose
        AND
        iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: 12 months

