SECURING ACCESS TO AFREZZA® FOR YOUR PATIENTS

afrezza® (insulin human) Inhalation Powder

Some insurance plans may require a **Prior Authorization (PA)** before approving the use of Afrezza.

Although coverage criteria for Afrezza may vary, the PA process is generally predictable across plans. To simplify the PA process, we have identified some helpful practices for healthcare providers.

The majority of Afrezza PAs will require the following information:

- Diagnosis of type 1 or type 2 diabetes
- Patient is 18 years or older
- Lung Function Test (FEV_1) baseline value and date of test
- No history of chronic lung disease, such as COPD or asthma
- Patient is a non-smoker or has not quit in the last 6 months

DOCUMENTATION FOR INSULIN EXPERIENCED PATIENTS

- Patient with type 1 diabetes is also on long-acting insulin
- Patient has tried another injectable rapid-acting insulin and experienced inadequate clinical results, such as:
  - No improvements in glycemic control
  - Increased side effects, such as hypoglycemia
  - Allergic reactions, such as injection site irritation
  - Lipohypertrophy

DOCUMENTATION FOR INSULIN NAIVE PATIENTS

- Patient has tried at least two oral glucose lowering agents
- Rationale for why the patient can't take the preferred rapid-acting injectable insulin, such as:
  - Fear of injections
  - Inability to self-administer injectable insulin, such as physical, mental, or visual impairment

Indications and Usage
Afrezza® (insulin human) Inhalation Powder is a rapid-acting inhaled insulin indicated to improve glycemic control in adult patients with diabetes mellitus.

Limitations of Use
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.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF ACUTE BRONCHOSPASM IN 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 (FEV_1) to identify potential lung disease in all patients.**

Contraindications
AFREZZA is contraindicated: during episodes of hypoglycemia, in patients with chronic lung disease (such as asthma or chronic obstructive pulmonary disease [COPD]) because of the risk of acute bronchospasm, and in patients with hypersensitivity to regular human insulin or any of the AFREZZA excipients.

Warnings and Precautions
Acute Bronchospasm: Acute bronchospasm has been observed following AFREZZA dosing in patients with asthma and COPD. Prior to initiating therapy, evaluate patients with a medical history, physical examination, and spirometry (FEV_1) to identify potential underlying lung disease. Do not use in patients with COPD.

Change in Insulin Regimen: Monitor blood glucose in all patients treated with insulin. Modify insulin regimen and dose cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type, or method of administration may result in the need for a change in insulin dose or an adjustment in concomitant oral antidiabetic treatment.

Hypoglycemia: Hypoglycemia is the most common adverse reaction of insulin therapy, including AFREZZA, and may be serious and life-threatening. Educate patients and caregivers on recognizing symptoms and mitigating the risks associated with hypoglycemia.

Decline in Pulmonary Function: AFREZZA has been shown to cause a decrease in lung function as measured by FEV_1. In clinical trials lasting up to 2 years, AFREZZA-treated patients experienced a small (40 mL) but greater FEV_1 decline than comparator-treated patients. Assess pulmonary function with spirometry at baseline, after the initial 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. Consider more frequent lung function assessment in patients with pulmonary symptoms, e.g., wheezing, bronchospasm, breathing difficulties, or persistent or recurring cough. If symptoms persist, discontinue AFREZZA.

Lung Cancer: In clinical trials, 2 cases of lung cancer were reported in patients exposed to AFREZZA while no cases were reported for the comparators. Two additional cases of lung cancer (squamous cell and lung blastoma) were reported in non-smokers exposed to AFREZZA after the trial completion. These data are insufficient to determine whether AFREZZA has an effect on lung or respiratory tract tumors. In patients with active lung cancer, a prior history of lung cancer, or in patients at risk of lung cancer, consider whether the benefits of AFREZZA outweigh the risks.

Diabetic Ketoacidosis (DKA): In clinical trials enrolling subjects with type 1 diabetes, diabetic ketoacidosis (DKA) was more common in subjects receiving AFREZZA (0.43%; n=13) than in subjects receiving comparators (0.14%; n=3). Increase the frequency of glucose monitoring and consider an alternate route of administration of insulin in patients at risk for DKA.

Hypersensitivity Reactions: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Discontinue AFREZZA, monitor, and treat if indicated.

Hypokalemia: All insulin products, including AFREZZA, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis,

OVERCOMING PAYER DENIALS FOR AFREZZA®

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When submitting an appeal to a payer, it helps to clearly and concisely describe the intended therapeutic outcome and potential consequences if the intervention is denied.

Although there is not a standardized process that applies across all payers when appealing a denial for Afrezza®, the goal is the same: **clinical justification of a patient's need and appropriateness for the therapy.**

Patient History

- **DISEASE AND TREATMENT HISTORY**
  Including failure with, or lack of response to, the preferred covered products. For example: no improvements in glycemic control, A1C, or time-in-range, increased side effects (such as hypoglycemia), and/or allergic reactions (such as injection-site irritation).
- **PATIENT INABILITY TO TAKE OR USE THE PREFERRED INJECTABLE RAPID-ACTING INSULIN**
  For example: fear of injections, physical inability to self-administer, lipohypertrophy, and or visual impairment.
- **HISTORY OF POSITIVE RESPONSES TO AFREZZA AND POTENTIAL CONSEQUENCES OF SWITCHING**
  For example: increased patient compliance, improvements in glycemic control, reduction in A1C, increased time-in-range, and decreased side effects, such as reduced rates of hypoglycemia.

Reason used to gain approval for Afrezza

For RAA Insulin where the preferred agent is failing the patient:

- Patient has patterns of post-prandial hyperglycemia
- Patient has a pattern of nocturnal Hypoglycemia
- Patient has hypoglycemia 2–4 hours after injection
- Patient's A1c not to goal / American Diabetes Association goal of <7%
- Patient has lipohypertrophy contributing to inconsistent meal-time injection absorption and unpredictable glucose control.

For the RAA Insulin Naive patient:

- Patient is unwilling or unable to "Self Inject" Rapid Acting Meal-time Insulin.
  - due to fear of needles / needle phobia.
  - due to lipohypertrophy

WE ARE HERE TO HELP

AfrezzaAssist® is a one-stop-hub solution that helps your patients get access to Afrezza and stay on therapy. Services include comprehensive reimbursement support and pharmacy fulfillment, as well as product training and support to help improve patient care.

TELEPHONE (TOLL-FREE)
1-844-323-7399

HOURS
Monday – Friday 8:00am – 8:00pm ET

IMPORTANT SAFETY INFORMATION (cont.)

ventricular arrhythmia, and death. Closely monitor potassium levels in patients at risk of hypokalemia and treat if indicated.

Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs): Fluid retention, which may lead to or exacerbate heart failure, can occur with concomitant use of TZDs and insulin. Observe these patients for signs and symptoms of heart failure. If heart failure occurs, consider dose reduction or discontinuation of TZD.

Drug Interactions
Certain drugs may affect glucose metabolism, increasing the risk of hypoglycemia or decreasing the blood glucose–lowering effect of AFREZZA. Dose adjustment and increased frequency of blood glucose monitoring may be required. Co-administration of beta-blockers, clonidine, guanethidine, and reserpine with AFREZZA may reduce the signs and symptoms of hypoglycemia. For full list, see Prescribing Information.

Adverse Reactions
The most common adverse reactions associated with AFREZZA include hypoglycemia, cough, and throat pain or irritation.

Please see full Prescribing Information for Afrezza, including BOXED WARNING, on Afrezza.com

References: 1. Data on file. MannKind Corporation. 2. Akturk GK, 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;20(10):639–647. 3. Seaquist ER, Blonde L, McGill JB, et al. Hypoglycaemia is reduced with use of inhaled Technosphere® Insulin relative to insulin aspart in type 1 diabetes mellitus. *Diabet Med.* 2020;37(5):752–759. 4. Afrezza (insulin human) Inhalation Powder Prescribing Information. MannKind Corporation.