Medication Guide
AFREZZA® (uh-FREZZ-uh)
(insulin human) inhalation powder

What is the most important information I should know about AFREZZA?
AFREZZA can cause serious side effects, including:

- **Sudden lung problems (bronchospasms). Do not use AFREZZA if you have long-term (chronic) lung problems such as asthma or chronic obstructive pulmonary disease (COPD).** Before starting AFREZZA, your healthcare provider will give you a breathing test to check how your lungs are working.

What is AFREZZA?

- AFREZZA is a man-made insulin that is breathed-in through your lungs (inhaled) and is used to control high blood sugar in adults with diabetes mellitus.
- AFREZZA is not for use in place of long-acting insulin. AFREZZA must be used with long-acting insulin in people who have type 1 diabetes mellitus.
- AFREZZA is not for use to treat diabetic ketoacidosis.
- It is not known if AFREZZA is safe and effective for use in people who smoke. AFREZZA is not for use in people who smoke or have recently stopped smoking (less than 6 months).
- It is not known if AFREZZA is safe and effective in children under 18 years of age.

Who should not use AFREZZA?
Do not use AFREZZA if you:

- have chronic lung problems such as asthma or COPD.
- are allergic to regular human insulin or any of the ingredients in AFREZZA. See the end of this Medication Guide for a complete list of ingredients in AFREZZA.

What should I tell my healthcare provider before using AFREZZA?
Before using AFREZZA, tell your healthcare provider about all your medical conditions, including if you:

- have lung problems such as asthma or COPD
- have or have had lung cancer
- are using any inhaled medications
- smoke or have recently stopped smoking
- have kidney or liver problems
- are pregnant, planning to become pregnant, or are breastfeeding. AFREZZA may harm your unborn or breastfeeding baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins or herbal supplements.
Before you start using AFREZZA, talk to your healthcare provider about low blood sugar and how to manage it.

How should I use AFREZZA?

- Read the detailed **Instructions for Use** that comes with your AFREZZA.
- Take AFREZZA exactly as your healthcare provider tells you to. Your healthcare provider should tell you how much AFREZZA to use and when to use it.
- Know the strength of AFREZZA you use. **Do not** change the amount of AFREZZA you use unless your healthcare provider tells you to.
- Take AFREZZA at the beginning of your meal.
- **Check your blood sugar levels.** Ask your healthcare provider what your blood sugar should be and when you should check your blood sugar levels.
- **Keep AFREZZA and all medicines out of the reach of children.**

Your dose of AFREZZA may need to change because of:

- Change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of other medicines you take.

What should I avoid while using AFREZZA?
While using AFREZZA do not:

- drive or operate heavy machinery, until you know how AFREZZA affects you
- drink alcohol or use over-the-counter medicines that contain alcohol
- smoke

What are the possible side effects of AFREZZA?

AFREZZA may cause serious side effects that can lead to death, including:

See "What is the most important information I should know about AFREZZA?"

- **low blood sugar (hypoglycemia).** Signs and symptoms that may indicate low blood sugar include:
  - dizziness or light-headedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability or mood change, hunger.
- **decreased lung function.** Your healthcare provider should check how your lungs are working before you start using AFREZZA, 6 months after you start using it and yearly after that.
- **lung cancer.** In studies of AFREZZA in people with diabetes, lung cancer occurred in a few more people who were taking AFREZZA than in people who were taking other diabetes medications. There were too few cases to know if lung cancer was related to AFREZZA. If you have lung cancer, you and your healthcare provider should decide if you should use AFREZZA.
- **diabetic ketoacidosis.** Talk to your healthcare provider if you have an illness. Your AFREZZA dose or how often you check your blood sugar may need to be changed.
- **severe allergic reaction (whole body reaction). Get medical help right away if you have any of these signs or symptoms of a severe allergic reaction:**
  - a rash over your whole body, trouble breathing, a fast heartbeat, or sweating.
- **low potassium in your blood (hypokalemia).**
- **heart failure.** Taking certain diabetes pills called thiazolidinediones or "TZDs" with AFREZZA may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with AFREZZA. Your healthcare provider should monitor you closely while you are taking TZDs with AFREZZA. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
  - shortness of breath, swelling of your ankles or feet, sudden weight gain.

  Treatment with TZDs and AFREZZA may need to be changed or stopped by your healthcare provider if you have new or worse heart failure.

Get emergency medical help if you have:

- trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

The most common side effects of AFREZZA include:

- low blood sugar (hypoglycemia), cough, sore throat

These are not all the possible side effects of AFREZZA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 (1-800-332-1088).

General information about the safe and effective use of AFREZZA.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use AFREZZA for a condition for which it was not prescribed. Do not give AFREZZA to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about AFREZZA. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about AFREZZA that is written for health professionals. For more information, go to www.AFREZZA.com or call **1-877-323-8505**.

What are the ingredients in AFREZZA?

Active ingredient: human insulin

Inactive ingredients: fumaryl diketopiperazine, polysorbate 80

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Registered trademark owned by MannKind Corporation
Patented: http://www.mannkindcorp.com/our-technology-patent-notices.htm
Distributed by:
MannKind Corporation™
MannKind Corporation™
Danbury, CT 06810

Instructions for Use

AFREZZA® (uh-FREZZ-uh)

(insulin human) inhalation powder

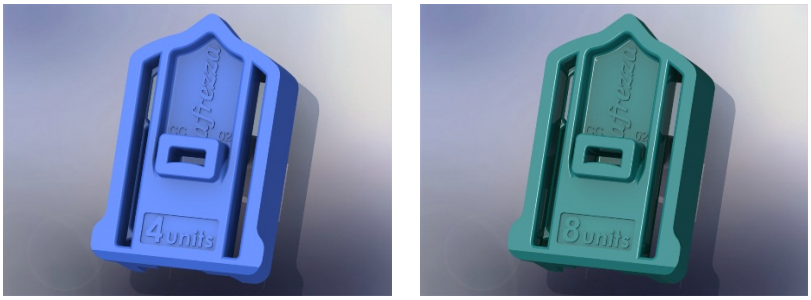
Read this Instructions for Use before you start using AFREZZA and each time you get a new AFREZZA inhaler. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Your healthcare provider should show you how to use your AFREZZA inhaler the right way before you use it for the first time.

Important information about AFREZZA:

- **AFREZZA comes in 2 strengths** (See Figure A):
  - 4 units (blue cartridge)
  - 8 units (green cartridge)

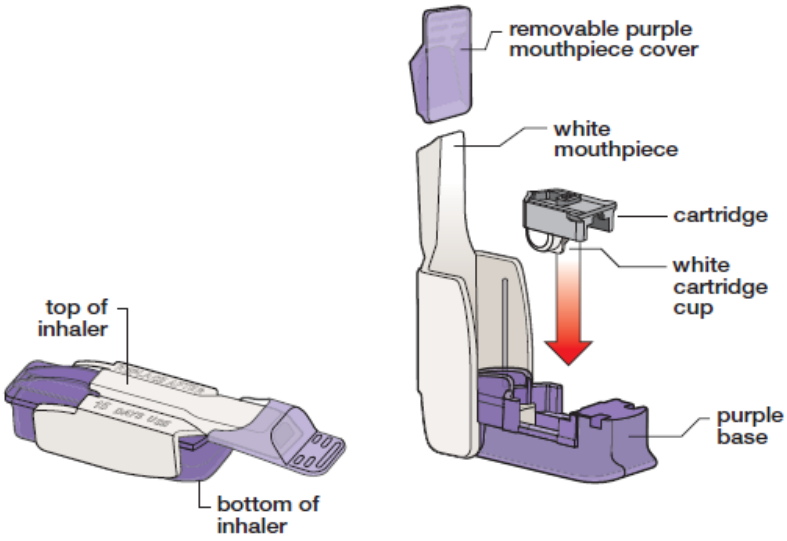
(Figure A)



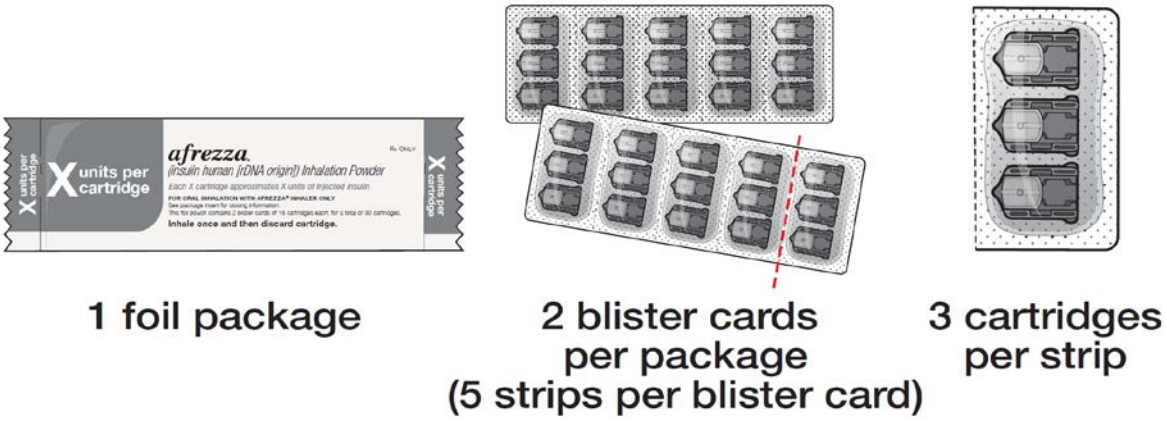
- If your prescribed AFREZZA dose is higher than 8 units, you will need to use more than 1 cartridge.
- If you need to use more than 1 cartridge for your dose, throw away the used cartridge before getting a new one. You can tell when a cartridge has been used, because the cup has moved to the center.
- **Do not try to open the AFREZZA cartridges.** The AFREZZA Inhaler opens the cartridge automatically during use.
- **AFREZZA cartridges should only be used with the AFREZZA Inhaler. Do not** try to breathe in the AFREZZA insulin powder in any other way. **Do not** put cartridges in your mouth and **do not** swallow cartridges.
- Use only 1 AFREZZA Inhaler at a time. The same inhaler should be used for the 4 unit or 8 unit cartridges.
- Throw away your AFREZZA Inhaler after 15 days and get a new one.

If you are having problems with your AFREZZA inhaler or if it breaks and you need a new one, call 1-877-323-8505.

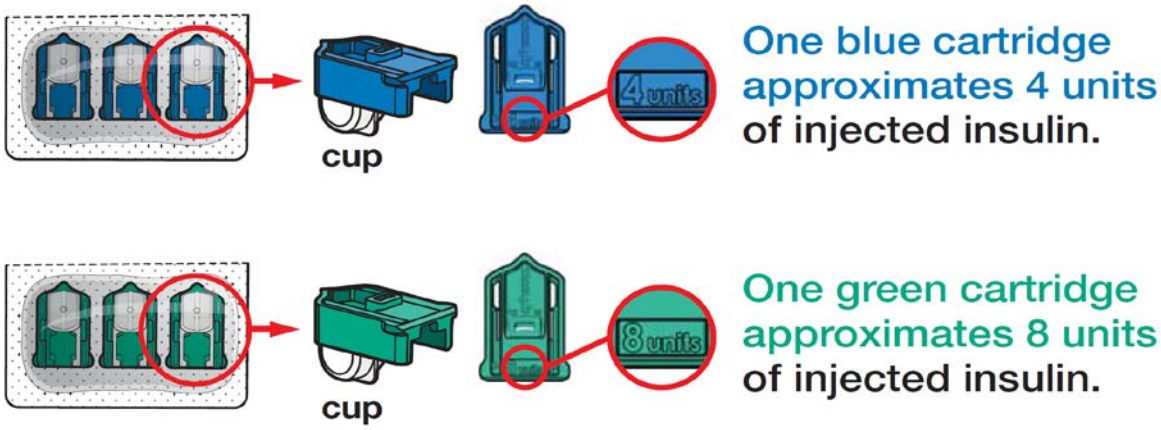
Know your AFREZZA® inhaler:



Know your AFREZZA® cartridges:



There are two strengths of AFREZZA® cartridges:

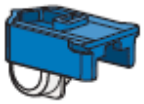


How to take your dose of AFREZZA:

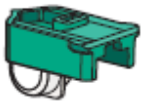
Always be sure you have the right number of AFREZZA cartridges for your dose available before you start. AFREZZA cartridges must only be used with the AFREZZA Inhaler.

Step 1: Select the AFREZZA cartridges for your dose

If your prescribed AFREZZA® dose is 4 units, use... 1 blue cartridge.



If your prescribed AFREZZA® dose is 8 units, use... 1 green cartridge.



If your prescribed AFREZZA® dose is more than 8 units you will need to use **more than 1 cartridge** to get your right dose.

Use the dosage chart below to determine the least number of AFREZZA® cartridges you can use for your dose. Other cartridge combinations can be used.

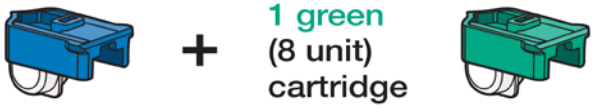
AFREZZA® Dose	# of **4 unit** (blue) cartridges needed	# of **8 unit** (green) cartridges needed
4 units		
8 units		
12 units	+	
16 units		
20 units	+	
24 units		

(Figure B)

Example:

If you need to take **12 units** of AFREZZA® you can use...

1 blue (4 unit) cartridge + 1 green (8 unit) cartridge



Select Cartridges

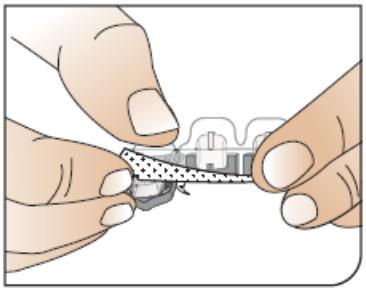
Important: Use the AFREZZA dose chart above (See Figure B) to help you choose the right number of AFREZZA cartridges needed for your dose.



Open Packages

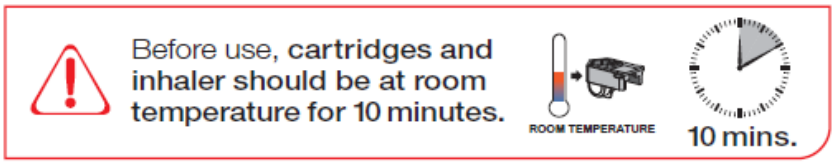
Remove a blister card from the foil package.

Tear along perforation to remove one strip.



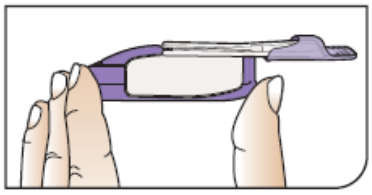
Push Cartridges to Remove

Remove a cartridge from the strip by pressing on the clear side to push the cartridge out. Remove the right number of cartridges for your dose. Pushing on the cup will not damage the cartridge. **AFREZZA cartridges left over in an opened strip must be used within 3 days.**



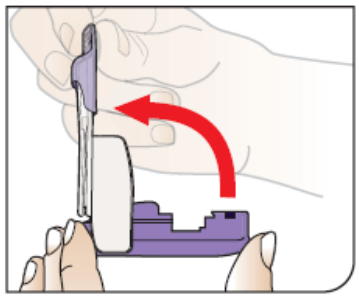
Before Proceeding:
Check that you have the right AFREZZA cartridge(s) for your dose.
Use only 1 inhaler for multiple cartridges. Throw away your AFREZZA inhaler after 15 days and get a new one.

Step 2: Loading a cartridge



Hold Inhaler

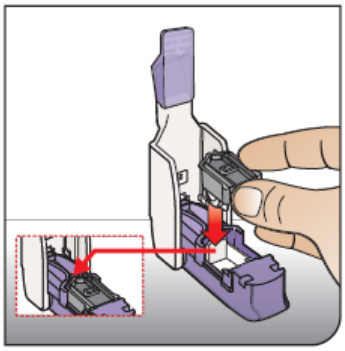
Hold the inhaler level in one (1) hand with the white mouthpiece on the top and purple base on the bottom.



Open Inhaler

Open the inhaler by lifting the white mouthpiece to a vertical position.

Before you put the AFREZZA cartridge in your inhaler, make sure it has been at **room temperature for 10 minutes**.

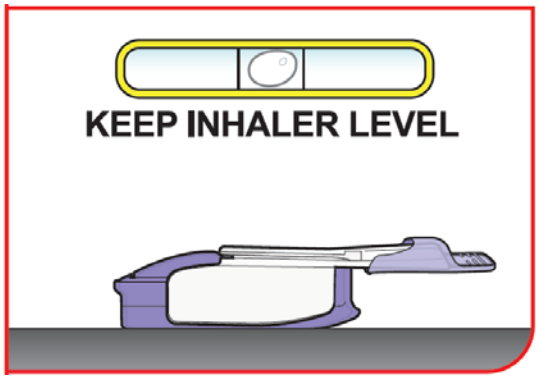


Place Cartridge

Hold the cartridge with the cup facing down.

Line up the cartridge with the opening in the inhaler. The pointed end of the cartridge should line up with the pointed end in the inhaler.

Place the cartridge into the inhaler. Be sure that the cartridge lies flat in the inhaler.



Keep Level Once Loaded!

Now that the cartridge is loaded, keep the inhaler level from this point forward to avoid loss of drug powder.



DO NOT turn inhaler upside down.



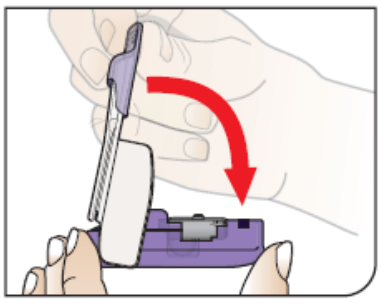
DO NOT point the mouthpiece down.



DO NOT shake or drop the inhaler.

This can result in loss of drug powder.

If any of these occur, throw away the cartridge and load a new cartridge.

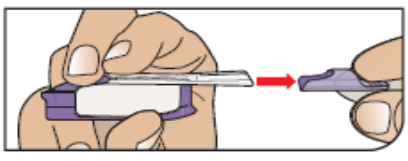


Close Inhaler

Lower the mouthpiece to close the inhaler (this will open the drug cartridge).

You should feel a snap when the inhaler is closed.

Step 3: Inhaling AFREZZA

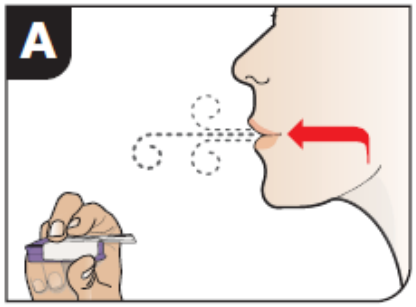


Remove the Mouthpiece Cover

Important: Keep the inhaler level during and after removal of the purple mouthpiece cover.

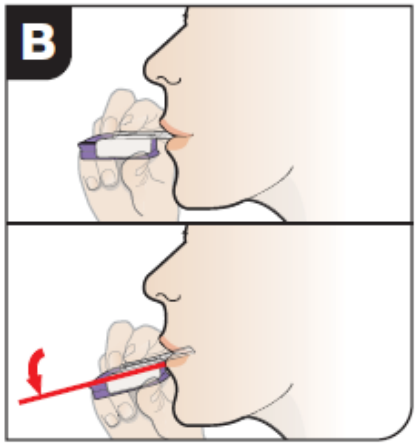
Check that you are ready to inhale:

- ✓ Purple mouthpiece cover is removed.
- ✓ Inhaler is held level.
- ✓ Fully review the following A-B-C steps prior to beginning the inhale process.



Exhale

Hold the inhaler away from your mouth and fully blow out (exhale).

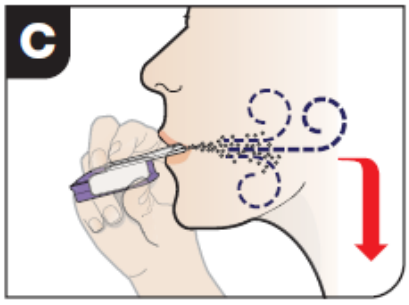


Position Inhaler in Mouth

Keeping your head level, place the mouthpiece in your mouth and **tilt the inhaler down towards your chin, as shown.**

Close your lips around the mouthpiece to form a seal.

Tilt the inhaler downward while keeping your head level.

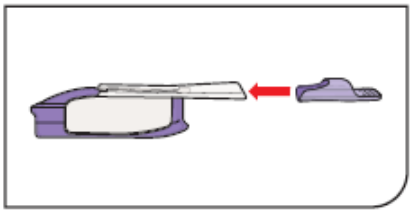


Inhale Deeply and Hold Breath

With your mouth closed around the mouthpiece, **inhale deeply through the inhaler**.

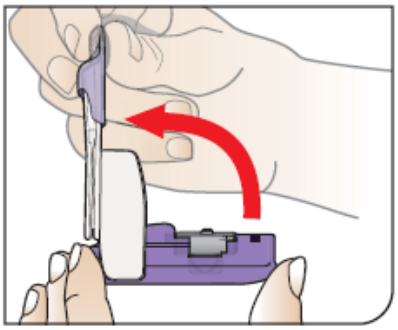
Hold your breath for as long as comfortable and at the same time remove the inhaler from your mouth. After holding your breath, exhale and continue to breathe normally.

Step 4: Removing a used cartridge



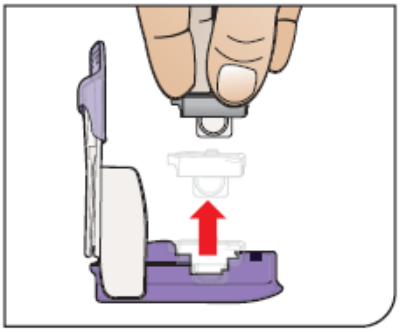
Replace Mouthpiece Cover

Place the purple mouthpiece cover back onto the inhaler.



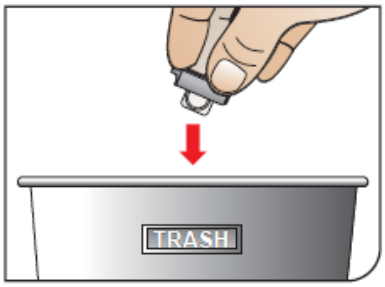
Open Inhaler

Open the inhaler by lifting up the white mouthpiece.



Remove Cartridge

Remove the cartridge from the purple base.

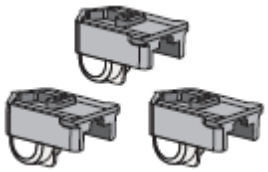


Throw away the Cartridge

Throw away the used cartridge in your regular household trash.

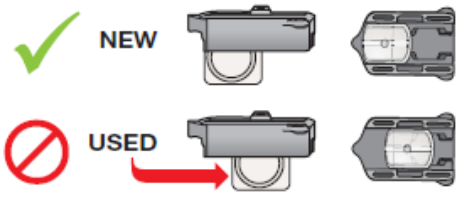
Multiple cartridge dosing

If you need more than one (1) AFREZZA cartridge for your dose, See the AFREZZA dosage chart above (Figure B).



Repeat steps 2 through 4 for each AFREZZA cartridge you need for your prescribed AFREZZA dose.

Be careful not to mix NEW cartridges with USED cartridges.



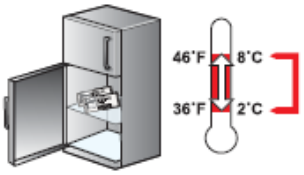
The white cup moves to the middle of the cartridge when it has been used.

How should I store AFREZZA?

Not In Use: Refrigerated Storage

Sealed Foil Packages

Store unopened drug in a refrigerator 36 – 46°F (2 – 8°C).



	Refrigerated
 Sealed (Unopened)	May be used until the **Expiration Date***

*If a foil package is not refrigerated, the contents must be used within 10 days.

In Use: Room Temperature Storage

Opened Foil Packages

Once a foil package has been opened, see chart below...

	Room Temperature
Blister Cards + Strips  Sealed (Unopened)	Must be used **within 10 Days**
Strips  Opened	Must be used **within 3 Days**

Before use, **cartridges and inhaler should be at room temperature for 10 minutes.**





Caring for your AFREZZA inhaler:

Storage Instructions

Once you have taken your full dose, make sure the purple mouthpiece cover has been replaced and the inhaler is closed.



- **Keep the inhaler in a clean, dry place** with the mouthpiece cover on until your next dose.
- May be stored refrigerated, but must be at room temperature before use.
- Never leave or store cartridges in the inhaler.
- Keep out of reach of children.

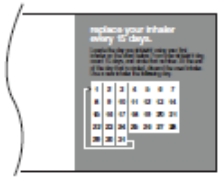
Care Instructions



EVERY 15 DAYS

- **Use one inhaler at a time. The same inhaler should be used to take 4 unit or 8 unit cartridges. Replace the inhaler every 15 days to maintain drug delivery.**

  Keep track of 15 days from when you start using the inhaler with a calendar, or use the chart on the back of the inhaler box.



- After taking your dose, powder residue in the mouthpiece is normal, this does not affect your dose.

  The outside of the inhaler can be wiped with a clean, dry cloth if needed. Never wash the inhaler. Keep it dry.

Switching between AFREZZA and injected insulin:

Contact your healthcare provide before switching insulins.
AFREZZA® is a mealtime insulin.
Do not switch from AFREZZA to a long acting insulin.
Do not switch from a long acting insulin to AFREZZA®.

To switch from AFREZZA® to injected mealtime insulin...



Find your AFREZZA® dose in the chart.

AFREZZA® Dose	# of **4 unit** (blue) cartridges needed	# of **8 unit** (green) cartridges needed	Injected Mealtime Insulin Dose
4 units			**4** units
8 units			**8** units
12 units	+		**12** units
16 units			**16** units
20 units	+		**20** units
24 units			**24** units

Find the correct dose of injected insulin.

If you cannot find your injected dose in the chart below, you must talk to a healthcare provider before using AFREZZA®.

To switch from injected mealtime insulin to AFREZZA®...



Find your injected insulin dose in the chart.

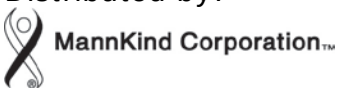
Injected Mealtime Insulin Dose	AFREZZA® Dose	# of **4 unit** (blue) cartridges needed	# of **8 unit** (green) cartridges needed
up to **4** units	**4** units		
5-8 units	**8** units		
9-12 units	**12** units	+	
13-16 units	**16** units		
17-20 units	**20** units	+	
21-24 units	**24** units		

Find the correct dose of AFREZZA®.

This Medication Guide and Instructions for Use has been approved by the U.S. Food and Drug Administration.

Patented: See http://www.mannkindcorp.com/our-technology-patent-notices.htm

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Approved: 6/2014