

PATIENT INFORMATION
BREZTRI AEROSPHERE™ (brez-TREE)
(budesonide, glycopyrrolate, and formoterol fumarate)
inhalation aerosol, for oral inhalation use

What is BREZTRI AEROSPHERE?

BREZTRI AEROSPHERE combines 3 medicines, an inhaled corticosteroid (ICS) medicine (budesonide), an anticholinergic medicine (glycopyrrolate), and a long-acting beta₂-adrenergic agonist (LABA) medicine (formoterol fumarate) in 1 inhaler, delivered as a propelled spray.

- ICS medicines such as budesonide help to decrease inflammation in the lungs. Inflammation in the lungs can lead to breathing problems.
- Anticholinergic medicines, such as glycopyrrolate and LABA medicines, such as formoterol fumarate help the muscles around the airways in your lungs stay relaxed to prevent symptoms, such as wheezing, cough, chest tightness, and shortness of breath. These symptoms can happen when the muscles around the airways tighten. This makes it hard to breathe.
- BREZTRI AEROSPHERE is a prescription medicine used long term to treat people with chronic obstructive pulmonary disease (COPD). COPD is a chronic lung disease that includes chronic bronchitis, emphysema, or both.
- BREZTRI AEROSPHERE is used as 2 inhalations, 2 times each day (2 puffs in the morning and 2 puffs in the evening) to improve symptoms of COPD for better breathing and to reduce the number of flare-ups (the worsening of your COPD symptoms for several days).
- **BREZTRI AEROSPHERE is not for the treatment of asthma.** It is not known if BREZTRI AEROSPHERE is safe and effective in people with asthma. BREZTRI AEROSPHERE contains formoterol fumarate. LABA medicines such as formoterol fumarate when used alone increase the risk of hospitalizations and death from asthma problems. BREZTRI AEROSPHERE contains an ICS, an anticholinergic, and a LABA. When an ICS and LABA are used together, there is not a significant risk in hospitalizations and deaths from asthma problems.
- **BREZTRI AEROSPHERE is not to be used to relieve sudden breathing problems** and will not replace a rescue inhaler. Always have a rescue inhaler (an inhaled, short-acting bronchodilator) with you to treat sudden breathing problems. If you do not have a rescue inhaler, contact your healthcare provider to have one prescribed for you.
- **BREZTRI AEROSPHERE should not be used in children.** It is not known if BREZTRI AEROSPHERE is safe and effective in children.

Do not use BREZTRI AEROSPHERE if you are allergic to budesonide, glycopyrrolate, formoterol, or any of the ingredients in BREZTRI AEROSPHERE. See “**What are the ingredients in BREZTRI AEROSPHERE?**” at the end of this Patient Information leaflet below for a complete list of ingredients in BREZTRI AEROSPHERE.

Before using BREZTRI AEROSPHERE, tell your healthcare provider about all of your medical conditions, including if you:

- have heart problems.
- have high blood pressure.
- have seizures.
- have thyroid problems.
- have diabetes.
- have liver problems.
- have kidney problems.
- have weak bones (osteoporosis).
- have an immune system problem.
- have eye problems such as glaucoma or cataracts. BREZTRI AEROSPHERE may make your glaucoma worse.
- have prostate or bladder problems, or problems passing urine. BREZTRI AEROSPHERE may make these problems worse.
- have any type of viral, bacterial, parasitic, or fungal infection.
- are exposed to chickenpox or measles.
- are pregnant or plan to become pregnant. It is not known if BREZTRI AEROSPHERE may harm your unborn baby.
- are breastfeeding. It is not known if the medicines in BREZTRI AEROSPHERE pass into your breast milk and if they can harm your baby. You and your healthcare provider should decide if you will take BREZTRI AEROSPHERE while breastfeeding.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. BREZTRI AEROSPHERE and certain other medicines may interact with each other. This may cause serious side effects.

Especially tell your healthcare provider if you take:

- anticholinergics (including tiotropium, ipratropium, aclidinium, and umeclidinium)
- other LABAs (including salmeterol, formoterol fumarate, arformoterol tartrate, vilanterol, olodaterol, and indacaterol)
- atropine
- antifungal or anti-HIV medicines

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist each time you get a new medicine.

How should I use BREZTRI AEROSPHERE?

Read the step-by-step instructions for using BREZTRI AEROSPHERE at the end of this Patient Information leaflet.

- Before using BREZTRI AEROSPHERE, make sure your healthcare provider has taught you how to use the inhaler and you understand how to use it correctly.
- Use BREZTRI AEROSPHERE exactly as your healthcare provider tells you to use it. **Do not** use BREZTRI AEROSPHERE more often than prescribed.
- Use 2 inhalations of BREZTRI AEROSPHERE, 2 times each day (2 puffs in the morning and 2 puffs in the evening).
- **Do not** take more than 2 inhalations of BREZTRI AEROSPHERE 2 times each day.
- If a dose (2 puffs) of BREZTRI AEROSPHERE is missed, it should be taken as soon as possible and the next dose should be taken at the usual time. Do not take more than one dose to make up for a forgotten dose.
- Rinse your mouth with water and spit the water out after each dose (2 puffs) of BREZTRI AEROSPHERE. Do not swallow the water. This will help to reduce the chance of getting a fungus infection (thrush) in the mouth and throat.
- If you take too much BREZTRI AEROSPHERE, call your healthcare provider or go to the nearest hospital emergency room right away if you have any unusual symptoms, such as worsening shortness of breath, chest pain, increased heart rate, or shakiness.
- **Do not** spray BREZTRI AEROSPHERE in your eyes. If BREZTRI AEROSPHERE gets in your eyes, rinse them well with water. If redness continues, call your healthcare provider.

- **Do not use other medicines that contain a LABA or an anticholinergic for any reason.** Ask your healthcare provider or pharmacist if any of your other medicines are LABA or anticholinergic containing medicines.
- Do not change or stop any medicines used to control or treat your breathing problems. Your healthcare provider will change your medicines as needed.
- **BREZTRI AEROSPHERE does not relieve sudden breathing problems and you should not take extra doses of BREZTRI AEROSPHERE to relieve sudden symptoms.** Always have a rescue inhaler with you to treat sudden symptoms. If you do not have a rescue inhaler, call your healthcare provider to have one prescribed for you.
- **Call your healthcare provider or get emergency medical care right away if:**
 - your breathing problems get worse.
 - you need to use your rescue inhaler more often than usual.
 - your rescue inhaler does not work as well to relieve your symptoms.

What are the possible side effects of BREZTRI AEROSPHERE?

BREZTRI AEROSPHERE can cause serious side effects, including:

- **fungal infection in your mouth or throat (thrush).** Rinse your mouth with water without swallowing after using BREZTRI AEROSPHERE to help reduce your chance of getting thrush.
- **pneumonia.** People with COPD have a higher chance of getting pneumonia. BREZTRI AEROSPHERE may increase your chance of getting pneumonia. Call your healthcare provider if you notice any of the following symptoms:
 - increase in mucus (sputum) production
 - change in mucus color
 - fever
 - chills
 - increased cough
 - increased breathing problems
- **weakened immune system and increased chance of getting infections (immunosuppression).**
- **reduced adrenal function (adrenal insufficiency).** Adrenal insufficiency is a condition where the adrenal glands do not make enough steroid hormones. This can happen when you stop taking oral corticosteroid medicines (such as prednisone) and start taking a medicine containing an ICS (such as BREZTRI AEROSPHERE). During this transition period, when your body is under stress from fever, trauma (such as a car accident), infection, surgery, or worse COPD symptoms, adrenal insufficiency can get worse and may cause death. Symptoms of adrenal insufficiency include:
 - feeling tired
 - lack of energy
 - weakness
 - nausea and vomiting
 - low blood pressure (hypotension)
- **sudden breathing problems immediately after inhaling your medicine.** If you have sudden breathing problems immediately after inhaling your medicine, stop taking BREZTRI AEROSPHERE and call your healthcare provider right away.
- **serious allergic reactions.** Call your healthcare provider or get emergency medical care if you get any of the following symptoms of a serious allergic reaction:
 - rash
 - hives
 - swelling of your face, mouth, and tongue
 - breathing problems
- **effects on your heart.**
 - increased blood pressure
 - a fast or irregular heartbeat
 - chest pain
- **effects on your nervous system.**
 - tremor
 - nervousness
- **bone thinning or weakness (osteoporosis).**
- **new or worsened eye problems including acute narrow-angle glaucoma and cataracts.** Acute narrow-angle glaucoma can cause permanent loss of vision if not treated. Symptoms of acute narrow-angle glaucoma may include:
 - eye pain or discomfort
 - nausea or vomiting
 - blurred vision
 - seeing halos or bright colors around lights
 - red eyes

If you have these symptoms, call your healthcare provider right away before taking another dose.

- **urinary retention.** People who take BREZTRI AEROSPHERE may develop new or worsening urinary retention. Symptoms of urinary retention may include:

- difficulty urinating
- urinating frequently
- painful urination
- urination in a weak stream or drips

If you have these symptoms of urinary retention, stop taking BREZTRI AEROSPHERE and call your healthcare provider right away before taking another dose.

- **changes in laboratory blood values,** including high levels of blood sugar (hyperglycemia) and low levels of potassium (hypokalemia). Low levels of potassium may cause symptoms of muscle spasm, muscle weakness, or abnormal heart rhythm.

Common side effects of BREZTRI AEROSPHERE include

- upper respiratory tract infection
- pneumonia
- back pain
- thrush in your mouth and throat. Rinse your mouth with water without swallowing after use to help prevent this.
- joint pain
- flu
- headache
- high blood sugar levels
- muscle spasms
- cough
- inflammation of the sinuses
- diarrhea
- hoarseness
- painful and frequent urination (signs of a urinary tract infection)
- nausea
- difficulty sleeping
- feeling anxious
- awareness of your heart beating (palpitations)

Tell your healthcare provider about any side effect that bothers you or that does not go away.

These are not all the possible side effects of BREZTRI AEROSPHERE. Ask your healthcare provider or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to AstraZeneca at 1-800-236-9933.

How should I store BREZTRI AEROSPHERE?

- Store BREZTRI AEROSPHERE at room temperature between 68°F to 77°F (20°C to 25°C). Keep in a dry place away from heat and sunlight.
- Store BREZTRI AEROSPHERE in the unopened foil pouch and only open when ready for use.
- **Do not** put a hole in the BREZTRI AEROSPHERE canister.
- **Do not** use or store BREZTRI AEROSPHERE near heat or a flame. Temperatures above 120°F (49°C) may cause the canister to burst.
- **Do not** throw the BREZTRI AEROSPHERE canister into a fire or an incinerator.
- Throw away BREZTRI AEROSPHERE 3 months after you open the foil pouch (for the 120-inhalation canister), or 3 weeks after you open the foil pouch (for the 28-inhalation canister), or when the dose indicator reaches zero “0”, whichever comes first.
- Keep BREZTRI AEROSPHERE and all medicines out of the reach of children.

General information about the safe and effective use of BREZTRI AEROSPHERE.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use BREZTRI AEROSPHERE for a condition for which it was not prescribed. Do not give your BREZTRI AEROSPHERE to other people, even if they have the same condition that you have. It may harm them.

You can ask your healthcare provider or pharmacist for information about BREZTRI AEROSPHERE that is written for healthcare professionals.

What are the ingredients in BREZTRI AEROSPHERE?

Active ingredients: micronized budesonide, micronized glycopyrrolate, and micronized formoterol fumarate

Inactive ingredients: hydrofluoroalkane (HFA 134a) and porous particles (comprised of DSPC [1,2-Distearoyl-*sn*-glycero-3-phosphocholine] and calcium chloride)

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Manufactured for: AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850; Manufactured by: AstraZeneca Dunkerque Production (AZDP), Dunkerque, France

For more information, go to www.BREZTRI.com or call 1-800-236-9933.