What is TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor)?

TRIKAFTA is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one copy of the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or another mutation that is responsive to treatment with TRIKAFTA.

Talk to your doctor to learn if you have an indicated CF gene mutation.

It is not known if TRIKAFTA is safe and effective in children under 6 years of age.

Please see Important Safety Information for TRIKAFTA on pages 5-7 and full Prescribing Information, including Patient Information.
How does TRIKAFTA work?

Please see Important Safety Information for TRIKAFTA on pages 5-7 and full Prescribing Information, including Patient Information.
WHO IS TRIKAFTA® FOR?

There are 178 mutations that are responsive to TRIKAFTA. To find out if you have a responsive mutation, visit TRIKAFTAEligibility.com.

TRIKAFTA IS APPROVED FOR PEOPLE WITH CF AGE 6+

with at least one F508del mutation or at least one other mutation* that is responsive to treatment with TRIKAFTA

*Predicted to respond to TRIKAFTA based on results in a laboratory setting. Not clinically evaluated.

TRINA AND TREY LEARN ABOUT TRIKAFTA

When Trina and Trey found out they were eligible for TRIKAFTA, they wanted to learn about it. Read about their adventures together with your child.

Visit ExploreTRIKAFTA.com

Please see Important Safety Information for TRIKAFTA on pages 5-7 and full Prescribing Information, including Patient Information.
The underlying cause

CF is caused by mutations in the CF gene. These mutations lead to defects in a specific protein called the cystic fibrosis transmembrane conductance regulator (CFTR) protein. As a result of these defects, the CFTR proteins don’t work the way they should.

CF gene mutations cause one or both defects illustrated below:

Defect 1:
Fewer CFTR proteins get to the cell surface, where they are normally located.

Defect 2:
CFTR proteins don’t open correctly if they do reach the cell surface.

Because of these defects, chloride ions cannot move into or out of the cells like they should. This can cause thick, sticky mucus to build up in organs, such as the lungs.

TRIKAFTA: Three components that work together to target the underlying cause

TRIKAFTA adds elexacaftor to tezacaftor and ivacaftor to target CFTR protein defects caused by the F508del mutation or another mutation responsive to TRIKAFTA.

By binding to different places on CFTR proteins, elexacaftor and tezacaftor work together to help more proteins reach the cell surface.

ivacaftor helps CFTR proteins stay open longer at the cell surface.

Together, the 3 components help responsive CFTR proteins function better.

What is known about how TRIKAFTA works was learned from studies conducted in a laboratory. Keep in mind that results from laboratory studies do not always match how these medicines work in a person. If you have questions about your treatment, speak with your healthcare provider.

Please see Important Safety Information for TRIKAFTA on pages 5-7 and full Prescribing Information, including Patient Information.
**Who should not take TRIKAFTA®?**

Do not take TRIKAFTA if you take certain medicines such as:

- antibiotics such as rifampin (RIFAMATE®, RIFATER®) or rifabutin (MYCOBUTIN®)
- seizure medicines such as phenobarbital, carbamazepine (TEGRETOL®, CARBATROL®, EQUETRO®), or phenytoin (DILANTIN®, PHENYTEK®)
- St. John’s wort

Talk to your doctor before taking TRIKAFTA if you take any of the medicines or herbal supplements listed above.

**What should I tell my doctor about my medical conditions before starting TRIKAFTA?**

Before taking TRIKAFTA, tell your doctor about all of your medical conditions, including if you:

- have kidney problems
- have or have had liver problems
- are pregnant or plan to become pregnant. It is not known if TRIKAFTA will harm your unborn baby. You and your doctor should decide if you will take TRIKAFTA while you are pregnant
- are breastfeeding or planning to breastfeed. It is not known if TRIKAFTA passes into your breast milk. You and your doctor should decide if you will take TRIKAFTA while you are breastfeeding

**Are there any other medicines that may interact with TRIKAFTA?**

TRIKAFTA may affect the way other medicines work, and other medicines may affect how TRIKAFTA works.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. The dose of TRIKAFTA may need to be adjusted when taken with certain medicines.

Ask your doctor or pharmacist for a list of these medicines if you are not sure. Make sure the list includes medicines from all your pharmacies, if you have more than one.

Especially tell your doctor if you take:

- antifungal medicines including ketoconazole (such as NIZORAL®), itraconazole (such as SPORANOX®), posaconazole (such as NOXAFIL®), voriconazole (such as VFEND®), or fluconazole (such as DIFLUCAN®)
- antibiotics including telithromycin (such as KETEK®), clarithromycin (such as BIAxin®), or erythromycin (such as ERY-TAB®)
- other medicines including rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John’s wort

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

Please see additional Important Safety Information for TRIKAFTA on pages 6-7 and full Prescribing Information, including Patient Information.
What are the possible side effects of TRIKAFTA? 

TRIKAFTA can cause serious side effects, including:

- **Liver damage and worsening of liver function** in people with severe liver disease that can be serious and may require transplantation. Liver damage has also happened in people without liver disease.

- **High liver enzymes in the blood** is a common side effect in people treated with TRIKAFTA. These can be serious and may be a sign of liver injury. Your doctor will do blood tests to check your liver:
  - before you start TRIKAFTA
  - every 3 months during your first year of taking TRIKAFTA
  - every year while you are taking TRIKAFTA

Your doctor may do blood tests to check the liver more often if you have had high liver enzymes in your blood in the past.

Call your doctor right away if you have any of the following symptoms of liver problems:

- pain or discomfort in the upper right stomach (abdominal) area
- yellowing of your skin or the white part of your eyes
- loss of appetite
- nausea or vomiting
- dark, amber-colored urine

- **Abnormality of the eye lens (cataract)** has happened in some children and adolescents treated with TRIKAFTA. If you are a child or adolescent, your doctor should perform eye examinations before and during treatment with TRIKAFTA to look for cataracts.

Your healthcare provider will monitor you for side effects. Be sure to call your healthcare provider if you have any questions.
What were the most common side effects seen with TRIKAFTA®?

This information is based on what was reported in a study of people age 12 years and older with one copy of the F508del mutation and another mutation defined in the study.*

<table>
<thead>
<tr>
<th>Side effect</th>
<th>TRIKAFTA (n=202)</th>
<th>Placebo (n=201)</th>
<th>Side effect</th>
<th>TRIKAFTA (n=202)</th>
<th>Placebo (n=201)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>17%</td>
<td>15%</td>
<td>Increase in a blood enzyme called creatine phosphokinase (CPK)†</td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>Upper respiratory tract infection (common cold)</td>
<td>16%</td>
<td>12%</td>
<td>Increase in a liver enzyme called aspartate aminotransferase (AST)†</td>
<td>9%</td>
<td>2%</td>
</tr>
<tr>
<td>Stomach (abdominal) pain</td>
<td>14%</td>
<td>9%</td>
<td>Runny nose</td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13%</td>
<td>7%</td>
<td>Stuffy nose</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>Rash</td>
<td>10%</td>
<td>5%</td>
<td>Flu (influenza)</td>
<td>7%</td>
<td>1%</td>
</tr>
<tr>
<td>Increase in a liver enzyme called alanine aminotransferase (ALT)†</td>
<td>10%</td>
<td>3%</td>
<td>Inflamed sinuses</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>9%</td>
<td>7%</td>
<td>Increase in blood bilirubin†</td>
<td>5%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Most common side effects experienced in a 24-week study in people taking TRIKAFTA compared with those taking placebo

The safety of TRIKAFTA observed in children with CF age 6 through 11 years was similar to what was observed in the study of people with CF age 12 years and older.‡

These are not all the possible side effects of TRIKAFTA. Call your doctor for medical advice about side effects. You are encouraged to report side effects to FDA at 1-800-FDA-1088.

*Mutations that either do not make a CFTR protein or make a protein that tezacaftor and/or ivacaftor cannot act on.
†Elevated levels of these blood tests could mean there is liver irritation or injury.
‡This enzyme is measured to help determine if there has been irritation to muscles.
§These people had one copy of the F508del mutation and another mutation defined in the study.

Please see additional Important Safety Information for TRIKAFTA on pages 5-6 and full Prescribing Information, including Patient Information.
How was TRIKAFTA studied?
The primary purpose of this study was to determine the safety and tolerability of TRIKAFTA. In addition, there were other study results. See page 9.

66 children with CF age 6 through 11 years with one copy of the F508del mutation and a mutation defined in the study* or two copies of the F508del mutation participated in the 24-week safety study.

Each child took TRIKAFTA every 12 hours with fat-containing food for 24 weeks (~6 months).
- All participants knew they were taking TRIKAFTA, and no children in the study took placebo
- Each participant’s dose of TRIKAFTA was based on their weight. For more information, see page 18
- All participants continued to take their other prescribed CF therapies

*Smutations that either do not make a CFTR protein or make a protein that tezacaftor and/or ivacaftor cannot act on.

Safety study results
FOR CHILDREN WITH CF AGE 6-11 YEARS
THE SAFETY OF TRIKAFTA OBSERVED IN THE STUDY WAS SIMILAR TO WHAT WAS OBSERVED IN PEOPLE WITH CF AGE 12+

Please see pages 5-7 for Important Safety Information and for side effects in people with CF age 12 years and older.
SAFETY STUDY RESULTS: CHILDREN WITH CF AGE 6 THROUGH 11 YEARS

Study considerations
Because no one took placebo in the safety study, it is not known if changes seen in the study were due to TRIKAFTA.

Keep in mind that all results shown are an average of all people studied and differed among individuals and mutations. Your child may have a different experience.

This study took place during the COVID-19 pandemic. As a result, Vertex put in place certain processes and guidelines during the study. Talk to your healthcare provider if you have any questions.

Additional safety study results

Lung function (FEV₁*) increased by 10.2 percentage points on average through 24 weeks.
On average, children in the study started with an FEV₁ of 88.8%.

*FEV₁=forced expiratory volume, or how much air a person can exhale in a forced breath in 1 second.

Sweat chloride decreased by 60.9 mmol/L on average through 24 weeks.
On average, children started the study with a sweat chloride level of 102.2 mmol/L.
Sweat chloride is a measure of the amount of salt in a person’s sweat.

Respiratory symptom score increased by 7 points on average through 24 weeks.
On average, children began the study with a score of 80.3 points.

Respiratory symptoms that were measured include cough, difficulty breathing, wheezing, congestion, mucus production, and waking up from coughing.
Respiratory symptoms were measured using a tool called the Cystic Fibrosis Questionnaire-Revised Respiratory Domain (CFQ-R) score.
The average increase in CFQ-R score means that, overall, the symptoms studied have improved. It does not mean there was an improvement in each symptom measured.

Body mass index (BMI†) increased by 1 kg/m² on average at 24 weeks.
For example, a child age 9 starting with a BMI around the 60th percentile would increase to around the 70th percentile.

†BMI=a measure of someone’s weight in relation to their height.
How was TRIKAFTA® studied?

This study was designed to determine the possible benefits and risks of TRIKAFTA compared with placebo. All people in this study had one copy of the F508del mutation. “A mutation defined in the study” refers to mutations that either do not make a CFTR protein or make a protein that tezacaftor and/or ivacaftor cannot act on.

403 people with CF, 12 years and older, with one copy of the F508del mutation and a mutation defined in the study, participated in the 24-week study.

200 took TRIKAFTA with fat-containing food.
Two tablets, each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg in the morning, and 1 tablet containing ivacaftor 150 mg in the evening about 12 hours later.

203 took placebo twice daily with fat-containing food about 12 hours apart.

All participants continued to take their other prescribed CF therapies.
At 4 weeks, lung function (FEV₁*) improved significantly

ON AVERAGE, FOR PEOPLE TAKING TRIKAFTA®
LUNG FUNCTION INCREASED BY

13.8 PERCENTAGE POINTS
VS PLACEBO

Lung function (FEV₁*) improvement was maintained through 24 weeks

TRIKAFTA  PLACEBO

The study results of TRIKAFTA are an average of all people studied and differed among individuals. Your experience may be different.

*FEV₁=forced expiratory volume, or how much air a person can exhale in a forced breath in 1 second.

Please see Important Safety Information for TRIKAFTA on pages 5-7 and full Prescribing Information, including Patient Information.
Decrease in sweat chloride

Significant decrease of 41.2 mmol/L on average compared with placebo at 4 weeks. Results were maintained throughout the study, with a decrease of 41.8 mmol/L on average compared with placebo through 24 weeks.

On average, people taking TRIKAFTA started the study with a sweat chloride level of 102.3 mmol/L. Sweat chloride is a measure of the amount of salt in a person's sweat.

The study results of TRIKAFTA are an average of all people studied and differed among individuals. Your experience may be different.

Fewer pulmonary exacerbations

Through 24 weeks, the number of pulmonary exacerbations significantly decreased by 63% for people taking TRIKAFTA® compared with placebo.

There were 41 pulmonary exacerbations in the TRIKAFTA group and 113 in the placebo group. Pulmonary exacerbations are changes in certain symptoms that require treatment with new oral, intravenous (IV), or inhaled antibiotics.

Additional pulmonary exacerbation results

71% fewer pulmonary exacerbations that led to hospitalizations through 24 weeks.
• 9 in the TRIKAFTA group and 32 in the placebo group

78% fewer pulmonary exacerbations that led to IV antibiotics through 24 weeks.
• 11 in the TRIKAFTA group and 51 in the placebo group

This study was not designed to determine whether these changes were because of TRIKAFTA. These additional results are not included in the full Prescribing Information for TRIKAFTA.
Improvement in CF respiratory symptoms
People taking TRIKAFTA® reported a significant 20.1-point average increase in CF respiratory symptom score compared with placebo at 4 weeks. Results were maintained throughout the study, with an increase of 20.2 points on average compared with placebo through 24 weeks.

On average, people taking TRIKAFTA began the study with a score of 68.3 points.
Respiratory symptoms were measured using a tool called the Cystic Fibrosis Questionnaire-Revised Respiratory Domain (CFQ-R) score.
The average increase in CFQ-R score means that, overall, the symptoms studied have improved. It does not mean there was an improvement in each symptom measured.

Increase in body mass index (BMI*)
Significant BMI increase of 1 kg/m² on average compared with placebo at 24 weeks.
For example, a person who is 5’5” and weighs 130 pounds would gain about 6 pounds on average at 24 weeks.
*BMI=a measure of someone’s weight in relation to their height.

The study results of TRIKAFTA are an average of all people studied and differed among individuals. Your experience may be different.
How was TRIKAFTA® studied?

This study was designed to determine the possible benefits and risks of TRIKAFTA compared with SYMDEKO® (tezacaftor/ivacaftor and ivacaftor), a prescription medicine used for the treatment of people with CF with two F508del mutations.

107 people with CF, 12 years and older, with two copies of the F508del mutation, participated in the study.

For the first 4 weeks, everyone took SYMDEKO. Then, participants were randomly split into 2 groups:

- 55 switched to TRIKAFTA for 4 weeks. Participants took TRIKAFTA with fat-containing food.
  
  Two tablets, each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg in the morning, and 1 tablet containing ivacaftor 150 mg in the evening about 12 hours later

- 52 continued taking SYMDEKO for 4 more weeks. Participants took SYMDEKO with fat-containing food.
  
  One tablet containing tezacaftor 100 mg/ivacaftor 150 mg in the morning, and 1 tablet containing ivacaftor 150 mg in the evening about 12 hours later

All participants discontinued any previous CFTR modulators but continued to take their other prescribed CF therapies.
Significant improvement in lung function (FEV₁*)

107 people took SYMDEKO for 4 weeks. At baseline, participants were randomly split into 2 groups: 55 switched to TRIKAFTA and 52 continued taking SYMDEKO for 4 more weeks.

The study results of TRIKAFTA are an average of all people studied and differed among individuals. Your experience may be different.

*FEV₁ = forced expiratory volume, or how much air a person can exhale in a forced breath in 1 second.
Decrease in sweat chloride

**Significant decrease of 45.1 mmol/L** on average compared with SYMDEKO* (tezacaftor/ivacaftor and ivacaftor) at 4 weeks.

On average, people taking TRIKAFTA* started the study with a sweat chloride level of 91.4 mmol/L. Sweat chloride is a measure of the amount of salt in a person’s sweat.

Improvement in CF respiratory symptoms

People taking TRIKAFTA reported a **significant 17.4-point average increase** in CF respiratory symptom score compared with SYMDEKO at 4 weeks.

On average, people taking TRIKAFTA began the study with a score of 70.6 points.

Respiratory symptoms were measured using a tool called the Cystic Fibrosis Questionnaire-Revised Respiratory Domain (CFQ-R) score.

The average increase in CFQ-R score means that, overall, the symptoms studied have improved. It does not mean there was an improvement in each symptom measured.

The study results of TRIKAFTA are an average of all people studied and differed among individuals. Your experience may be different.

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Please see Important Safety Information on pages 5-7 for TRIKAFTA and on pages 20-21 for SYMDEKO. Please see TRIKAFTA full Prescribing Information, including Patient Information. Please see SYMDEKO full Prescribing Information, including Patient Information.
How is TRIKAFTA packaged?

**For children age 6 through 11 years weighing less than 30 kg (66 lbs)**

- Each box of TRIKAFTA has 4 weekly blister cards
- Each blister card contains 21 tablets:
  - 2 light orange tablets for each morning
  - 1 light blue tablet for each evening

**For children age 6 through 11 years weighing 30 kg (66 lbs) or more and people age 12 years and older**

- Each box of TRIKAFTA has 4 weekly blister cards
- Each blister card contains 21 tablets:
  - 2 orange tablets for each morning
  - 1 light blue tablet for each evening

Here are illustrations of the TRIKAFTA tablets next to an illustration of a pistachio.

**The light orange tablet is approximately 12 mm by 6 mm.**

**The light blue tablet is approximately 13 mm by 7 mm.**

Talk to your healthcare provider about all of the medicines you take, as the dose of TRIKAFTA may need to be adjusted.

It’s important to take TRIKAFTA exactly as your healthcare provider tells you.

Please see Important Safety Information for TRIKAFTA on pages 5-7 and full Prescribing Information, including Patient Information.
What is the recommended dose?
Your doctor will prescribe TRIKAFTA based on your age and weight.

<table>
<thead>
<tr>
<th>Age/Weight</th>
<th>Morning Dose</th>
<th>Evening Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>For children age 6 through 11 years weighing less than 30 kg (66 lbs)</td>
<td>Two light orange tablets (elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 75 mg) with fat-containing food</td>
<td>About 12 hours later One light blue tablet (ivacaftor 75 mg) with fat-containing food</td>
</tr>
<tr>
<td>For children age 6 through 11 years weighing 30 kg (66 lbs) or more—and—people age 12 years and older</td>
<td>Two orange tablets (elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) with fat-containing food</td>
<td>About 12 hours later One light blue tablet (ivacaftor 150 mg) with fat-containing food</td>
</tr>
</tbody>
</table>

Each dose must be taken with fat-containing food

- Always take TRIKAFTA with a meal or snack that contains fat to help your body absorb the medicine
- Examples of fat-containing foods include butter, peanut butter, eggs, nuts, meat, and whole-milk dairy products such as whole milk, cheese, and yogurt

Every dose matters

Make sure to take every dose of TRIKAFTA exactly as prescribed by your healthcare provider. Because the 3 components of TRIKAFTA work together to treat the underlying cause, each and every dose matters.

Talk to your healthcare provider about all of the medicines you take, as the dose of TRIKAFTA may need to be adjusted.

Avoid foods and drinks that contain grapefruit while taking TRIKAFTA because they may affect the amount of TRIKAFTA in your body.

Please see Important Safety Information for TRIKAFTA on pages 5-7 and full Prescribing Information, including Patient Information.
I MISSED A DOSE—WHAT SHOULD I DO?

**What to do if a morning dose was missed**

If it’s been 6 hours or LESS since the morning dose is usually taken:
- **Take the missed dose** with fat-containing food as soon as possible
- Then take the next dose at the usual time with fat-containing food

If it’s been MORE than 6 hours since the morning dose is usually taken:
- **Take the missed dose** with fat-containing food as soon as possible
- **Then do not take the evening dose.** Resume regular dosing schedule the next day

**What to do if an evening dose was missed**

If it’s been 6 hours or LESS since the evening dose is usually taken:
- **Take the missed dose** with fat-containing food as soon as possible
- Then take the next dose at the usual time with fat-containing food

If it’s been MORE than 6 hours since the evening dose is usually taken:
- **Do not take the missed dose**
- Take the next morning dose at the usual time with fat-containing food

**Do not take more than your usual dose of TRIKAFTA® to make up for a missed dose.**

Trina and Trey Learn How to Take TRIKAFTA

Our Trilandia explorers are ready to set out on an adventure to help you and your child learn about taking TRIKAFTA.

Visit [HowToTakeTRIKAFTA.com](http://HowToTakeTRIKAFTA.com)
What is SYMDEKO?
SYMDEKO is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have two copies of the F508del mutation, or who have at least one mutation in the CF gene that is responsive to treatment with SYMDEKO.

Talk to your doctor to learn if you have an indicated CF gene mutation.

It is not known if SYMDEKO is safe and effective in children under 6 years of age.

Important Safety Information
Do not take SYMDEKO if you take certain medicines or herbal supplements such as:

- antibiotics such as rifampin (RIFAMATE®, RIFATER*) or rifabutin (MYCOBUTIN*)
- seizure medicines such as phenobarbital, carbamazepine (TEGRETOL®, CARBATROL®, EQUETRO*), or phenytoin (DILANTIN®, PHENYTEK*)
- St. John's wort

Talk to your doctor before taking SYMDEKO if you take any of the medicines or herbal supplements listed above.

Before taking SYMDEKO, tell your doctor about all of your medical conditions, including if you:

- have or have had liver problems
- have kidney problems
- are pregnant or plan to become pregnant. It is not known if SYMDEKO will harm your unborn baby. You and your doctor should decide if you will take SYMDEKO while you are pregnant
- are breastfeeding or planning to breastfeed. It is not known if SYMDEKO passes into your breast milk. You and your doctor should decide if you will take SYMDEKO while you are breastfeeding

SYMDEKO may affect the way other medicines work, and other medicines may affect how SYMDEKO works.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements, because the dose of SYMDEKO may need to be adjusted when taken with certain medicines. Especially tell your doctor if you take:

- antifungal medicines such as ketoconazole (e.g., NIZORAL®), itraconazole (e.g., SPORANOX®), posaconazole (e.g., NOXAFIL®), voriconazole (e.g., VFEND®), or fluconazole (e.g., DIFLUCAN®)
- antibiotics such as telithromycin (e.g., KETEK®), clarithromycin (e.g., BIAxin®), or erythromycin (e.g., ERY-TAB ™)

What should I avoid while taking SYMDEKO?

- SYMDEKO can cause dizziness in some people who take it. Do not drive a car, use machinery, or do anything that needs you to be alert until you know how SYMDEKO affects you
- Avoid food or drink that contains grapefruit while you are taking SYMDEKO
Important Safety Information for SYMDEKO® (Continued)

What are the possible side effects of SYMDEKO?

SYMDEKO can cause serious side effects, including:

- **High liver enzymes in the blood** have been reported in people treated with SYMDEKO or treated with ivacaftor alone. Your doctor will do blood tests to check your liver:
  - before you start SYMDEKO
  - every 3 months during your first year of taking SYMDEKO
  - every year while you are taking SYMDEKO

Your doctor may do blood tests to check the liver more often if you have had high liver enzymes in your blood in the past.

Call your doctor right away if you have any of the following symptoms of liver problems:
  - pain or discomfort in the upper right stomach (abdominal) area
  - yellowing of your skin or the white part of your eyes
  - loss of appetite
  - nausea or vomiting
  - dark, amber-colored urine

- **Abnormality of the eye lens (cataract)** in some children and adolescents treated with SYMDEKO or with ivacaftor alone. If you are a child or adolescent, your doctor should perform eye examinations before and during treatment with SYMDEKO to look for cataracts

The most common side effects of SYMDEKO include headache, nausea, sinus congestion, and dizziness.

These are not all the possible side effects of SYMDEKO. Call your doctor for medical advice about side effects. You are encouraged to report side effects to FDA at 1-800-FDA-1088.
Personalized support, right from the start of treatment
Support from Vertex GPS™: Guidance & Patient Support starts with our team of Patient Support Specialists.

Your dedicated Patient Support Specialist can help by:

- **Verifying coverage with your insurance company** to review your coverage and out-of-pocket costs
- **Connecting with your healthcare provider** to discuss any prior authorization (PA) requirements or questions your insurance company may have while determining your coverage
- **Providing financial assistance information.** If you have commercial insurance, Vertex may be able to help reduce your co-payment obligation to as little as $15 per refill.* Call your Patient Support Specialist at 1-877-752-5933 (press 2) to see if you’re eligible
  
  *Limitations apply, and Vertex reserves the right to rescind, revoke, or amend this assistance program at any time.
- **Working with your specialty pharmacy** to help you coordinate shipments and let you know when it’s time to refill your Vertex medicine
- **Continuing to support you** while you are taking a Vertex medicine by providing educational tools, text message refill reminders, and other helpful resources

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**Not enrolled in Vertex GPS?**
If you have been prescribed TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor), ask your healthcare provider about completing an enrollment form at your next appointment.

**Already enrolled?**
If you are currently enrolled in GPS, you can call or text your Patient Support Specialist at 1-877-752-5933 (press 2), Monday through Friday, from 8:30 AM to 7 PM ET.

Learn more about GPS and the support resources available at [VertexGPS.com](http://VertexGPS.com).

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**GET DELICIOUS RECIPES AND FOOD IDEAS**

VISIT CF KITCHEN ON [EVERYDAY-CF.COM](http://EVERYDAY-CF.COM)

- Filter recipes by type of meal and level of difficulty
- Find ways to take recipes to the next level
- Explore fresh tips for when you’re on the go

Everyday CF Your source for fresh insights, resources, and tips for supporting your life with CF.

Everyday-CF.com is an educational website developed by Vertex Pharmaceuticals Incorporated.
**SUMMARY OF TRIKAFTA® STUDIES**

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age 12 years and older</strong></td>
<td><strong>24-week study of F508del/a mutation defined in the study</strong>&lt;sup&gt;†&lt;/sup&gt;</td>
</tr>
<tr>
<td>TRIKAFTA compared to placebo</td>
<td></td>
</tr>
<tr>
<td><strong>On average, people taking TRIKAFTA experienced:</strong></td>
<td></td>
</tr>
<tr>
<td>Improvement in lung function (FEV&lt;sub&gt;1&lt;/sub&gt;)&lt;sup&gt;‡&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;, forced expiratory volume, or how much air a person can exhale in a forced breath in 1 second</td>
<td></td>
</tr>
<tr>
<td>Fewer pulmonary exacerbations</td>
<td></td>
</tr>
<tr>
<td>Pulmonary exacerbations are changes in certain symptoms that require treatment with new oral, iv, or inhaled antibiotics.</td>
<td></td>
</tr>
<tr>
<td>Decrease in sweat chloride</td>
<td></td>
</tr>
<tr>
<td>Measured through a sweat test that determines the amount of salt in your sweat</td>
<td></td>
</tr>
<tr>
<td>Reduction in CF respiratory symptoms</td>
<td></td>
</tr>
<tr>
<td>Respiratory symptoms were measured using a tool called the Cystic Fibrosis Questionnaire-Revised Respiratory Domain score.</td>
<td></td>
</tr>
<tr>
<td>Increase in body mass index (BMI)&lt;sup&gt;§&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>BMI=a measure of someone’s weight in relation to their height</td>
<td></td>
</tr>
</tbody>
</table>

*Mutations that either do not make a CFTR protein or make a protein that tezacaftor and/or ivacaftor cannot act on.

**In a study of children with CF age 6 to 11 years, the safety of TRIKAFTA observed was similar to what was seen in people age 12 years and older.**

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**Important Safety Information**

Do not take TRIKAFTA if you take certain medicines such as:

- antibiotics such as rifampin (RIFAMATE®, RIFATER®) or rifabutin (MYCOBUTIN®)
- seizure medicines such as phenobarbital, carbamazepine (TEGRETOL®, CARBATROL®, EQUETRO®), or phenytoin (DILANTIN®, PHENYTEK®)
- St. John’s wort

Talk to your doctor before taking TRIKAFTA if you take any of the medicines or herbal supplements listed above.

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**Additional Safety Information**

TRIKAFTA can cause serious side effects, including liver damage and worsening of liver function, high liver enzymes in the blood, and abnormality of the eye lens (cataract).

To learn more about the studies’ designs and results, see pages 8 through 16.

*Mutations that either do not make a CFTR protein or make a protein that tezacaftor and/or ivacaftor cannot act on.

Please see additional Important Safety Information on pages 5-7 for TRIKAFTA and Important Safety Information on pages 20-21 for SYMDEKO. Please see TRIKAFTA full Prescribing Information, including Patient Information. Please see SYMDEKO full Prescribing Information, including Patient Information.

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To learn more, talk to your healthcare provider and visit TRIKAFTA.com.