Since CF is working beneath the surface, your treatment should be, too. With SYMDEKO, you can target the underlying cause of your CF.

**WHAT IS SYMDEKO™ (tezacaftor/ivacaftor and ivacaftor)?**
SYMDEKO is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 12 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 12 years of age.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.
WHY SYMDEKO™?
For patients 12 years and older with certain mutations (see page 4).

EVEN ONE’S CF IS DIFFERENT.
but ultimately, CF still works beneath the surface.

SINCE CF IS WORKING BENEATH THE SURFACE,
your treatment should be, too.

SYMDEKO IS TOUGH ON CF
because it targets the underlying cause.

Start learning about SYMDEKO, the latest medication from Vertex for people with CF age 12 years and older with certain mutations (see page 4).

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.
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.

Please see additional Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.
THE UNDERLYING CAUSE OF CF

CF is caused by CFTR protein defects. A mutation in the genes of a person with CF may make defective CFTR proteins that:

- Don’t open correctly
- Don’t get to the cell surface, where they are normally located

A person with CF may make CFTR proteins that have one or both of these defects.

Because of these defects, chloride ions cannot flow freely into or out of the cells as they should. This can lead to thick, sticky mucus in the lungs.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.

SYMDEKO™ TARGETS THE UNDERLYING CAUSE OF CF

SYMDEKO is made up of tezacaftor and ivacaftor, which work on certain defects of the CFTR protein at the cellular level in patients 12 years and older.

Together, tezacaftor and ivacaftor help the CFTR proteins work better. This allows more chloride ions to pass into and out of the cells—helping keep a balance of salt and water in certain organs such as the lungs.

What is known about how SYMDEKO 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.
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®, Carbafol®, Equetro®) or phenytoin (Dilanit®, 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 breast feeding

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 or Seville oranges while you are taking SYMDEKO.

Please see additional Important Safety Information on pages 10-11 and full Prescribing Information, including Patient Information.
IMPORTANT SAFETY AND SIDE EFFECT INFORMATION FOR SYMDEKO™

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 in two different clinical studies include headache, nausea, sinus congestion, and dizziness.

<table>
<thead>
<tr>
<th>Most common side effects experienced</th>
<th>People taking SYMDEKO</th>
<th>People taking placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>13%</td>
<td>13%</td>
</tr>
<tr>
<td>Nausea</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Sinus congestion</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4%</td>
<td>2%</td>
</tr>
</tbody>
</table>

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.

Additional Safety Information

Respiratory events (breathing problems)
11.3% of people taking SYMDEKO experienced respiratory events such as chest tightness and difficulty breathing compared with 14.7% of people taking placebo.

People who stopped treatment
1.6% of people taking SYMDEKO stopped treatment due to side effects compared with 2.0% of people taking placebo.

Please see additional Important Safety Information on pages 8-9 and full Prescribing Information, including Patient Information.
STUDY DETAILS (STUDY 1)

This 24-week (6-month) clinical study included people age 12 years and older with 2 copies of the F508del mutation in the CF gene. SYMDEKO™ and placebo were compared to determine the possible benefits and risks of SYMDEKO.

- 248 people with CF took SYMDEKO and 256 took placebo every 12 hours with fat-containing food
- Participants continued to take their other prescribed CF therapies

Click to see study results on the next page.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.
PEOPLE WITH F508DEL/F508DEL
(STUDY 1)

Improved lung function by 4 percentage points on average compared with those who took placebo.

SYMDEKO™ SIGNIFICANTLY IMPACTED LUNG FUNCTION AND PULMONARY EXACERBATIONS

Improved lung function by 4 percentage points on average compared with those who took placebo.

**LUNG FUNCTION (FEV₁)**

Week 16

Day 1

Day 15

Symdeko

Placebo

% Point Change in Lung Function

95% Confidence Interval

Day 4

Day 8

Day 12

Day 24

Keep in mind, results shown are an average for all people studied and differed among individuals. Your experience may be different.

*FEV₁ = forced expiratory volume in 1 second.

ADDITIONAL CLINICAL STUDY RESULTS

PULMONARY EXACERBATIONS
through 24 weeks

Significantly lowered the chance of having a pulmonary exacerbation by 35% on average compared with those who took placebo.

**BODY MASS INDEX (BMI)**

at 24 weeks

Increased by 0.06 kg/m² on average compared with those who took placebo

- For example, a person who is 5’4” and 110 pounds would gain 0.35 pounds, or a person who is 5’10” and 160 pounds would gain 0.42 pounds
- It cannot be determined if this change was due to SYMDEKO

**CF RESPIRATORY SYMPTOMS**

through 24 weeks

5.1 point change in certain CF respiratory symptoms compared with those who took placebo

- It cannot be determined if this change was due to SYMDEKO

A tool† was used to measure CF respiratory symptoms including cough, difficulty breathing, and mucus production.

RESPIRATORY SYMPTOMS

†Respiratory symptoms were measured by the CFQ-R Respiratory Domain score, which is a tool used in research to measure CF respiratory symptom improvement.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.
PEOPLE WITH OTHER RESPONSIVE MUTATIONS

Here, we see a list of mutations responsive to SYMDEKO™ based on studies and clinical settings. These mutations were not included in the clinical study and are predicted to respond based on results from a laboratory setting.

### Laboratory setting
- A1067T
- E56K
- F1074L
- D110E
- E193K
- K1060T
- D1270N
- F1052V
- R74W

### Study 2 (clinical setting)
- 711+3A → G
- 2789+5G → A
- 3272-26A → G
- 3849+10kbC → T
- A455E
- D110H
- P67L
- S945L
- D1152H
- R347H
- E831X
- R352Q
- R352Q
- R1070W

These mutations were not included in the clinical study and are predicted to respond based on results from a laboratory setting.

### Study Details (Study 2)
In a clinical study of 244 people with CF, SYMDEKO was compared with ivacaftor alone and placebo to determine the possible benefits and risks of SYMDEKO. Participants were age 12 years and older with the F508del mutation and a second mutation in the CF gene predicted to respond to SYMDEKO.

- Each person had two 8-week treatment periods where they took either placebo, ivacaftor alone, or SYMDEKO every 12 hours with fat-containing food. Participants received two of the three possible treatments after completing both treatment periods.
- Between treatment periods there was an 8-week washout period where they did not take SYMDEKO, placebo, or ivacaftor.
- Participants continued to take their other prescribed CF therapies.

### Study Results
Click to see study results on the next page.

**PEOPLE WITH OTHER RESPONSIVE MUTATIONS** (STUDY 2)

Improved lung function overall by an average of 6.8 percentage points compared with placebo. Additionally, improved lung function by an average of 2.1 percentage points compared with ivacaftor alone.

*FEV₁ = forced expiratory volume in 1 second.

Changes in lung function varied by mutations (range -1.0 to 10.1 percentage points compared with placebo) and individuals.

**SYMDEKO™ SIGNIFICANTLY IMPACTED LUNG FUNCTION**

**SYMDEKO**

**CF RESPIRATORY SYMPTOMS**

A tool† was used to measure CF respiratory symptoms including cough, difficulty breathing, and mucus production.

Keep in mind, all results shown are an average of all people studied and differed among individuals and mutations. Your experience may be different.

†Respiratory symptoms were measured by the CFQ-R Respiratory Domain score, which is a tool used in research to measure CF respiratory symptom improvement.
IMPORTANT SAFETY AND SIDE EFFECT INFORMATION FOR SYMDEKO™

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., Noxafite®), 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 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.

Please see additional Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.
The recommended dose of SYMDEKO is:

Be sure to avoid foods and drinks that contain grapefruit or Seville oranges while taking SYMDEKO because they may affect the amount of SYMDEKO in the body.

HOW TO TAKE SYMDEKO™

It’s important to take SYMDEKO exactly as your healthcare provider tells you to take it, along with your other CF therapies. SYMDEKO should always be taken by mouth, along with fat-containing food.

The recommended dose of SYMDEKO is:

- **a morning** yellow (tezacaftor/ivacaftor) tablet  
  (12 hours later)  
- **an evening** light blue (ivacaftor) tablet

### SYMDEKO and fat-containing foods

Always take SYMDEKO with a fat-containing meal or snack to help your body absorb the medicine. You can find ideas for fat-containing foods on page 24 and on SYMDEKO.com.

Be sure to avoid foods and drinks that contain grapefruit or Seville oranges while taking SYMDEKO because they may affect the amount of SYMDEKO in the body.

**Every dose matters**

Together, the medicines that make up SYMDEKO target the underlying cause of CF. Talk to your healthcare provider about all of the medicines you take, as your dose of SYMDEKO may need to be adjusted. Be sure to take every dose exactly as prescribed by your healthcare provider, because every dose matters.

**If you miss a dose**

If you miss a dose of SYMDEKO and it is **6 hours or less** from the time you usually take your yellow tablet in the morning or the light blue tablet in the evening, **take the missed dose** with food that contains fat as soon as you can. Then take your next dose at your usual time.

If it is **more than 6 hours** from the time you usually take the yellow tablet in the morning or the light blue tablet in the evening, **do not take** the missed dose. Take your next dose at the usual time with food that contains fat. Do not take more than your usual dose of SYMDEKO to make up for a missed dose.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.
### IDEAS FOR FAT-CONTAINING FOODS

<table>
<thead>
<tr>
<th>If you have more time</th>
<th>If you’re in a rush</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BREAKFAST</strong></td>
<td></td>
</tr>
<tr>
<td>• Pancakes with pecans and berries</td>
<td>• Granola with whole milk</td>
</tr>
<tr>
<td>• Southwestern omelet</td>
<td>• Bagel with peanut butter</td>
</tr>
<tr>
<td><strong>SNACK</strong></td>
<td></td>
</tr>
<tr>
<td>• Smoothie with nut butter</td>
<td>• Trail mix</td>
</tr>
<tr>
<td>• Cream cheese fruit dip</td>
<td>• Whole milk string cheese</td>
</tr>
<tr>
<td><strong>DINNER</strong></td>
<td></td>
</tr>
<tr>
<td>• Lasagna</td>
<td>• Quesadilla with whole milk cheese and guacamole</td>
</tr>
<tr>
<td>• Chicken pot pie</td>
<td>• Sausage pizza</td>
</tr>
</tbody>
</table>

Keep in mind, this list is meant to provide you with a range of options, but is not intended to be a complete list of foods. Your healthcare team can help you choose the right fat-containing meals and snacks for you.

Looking for new and delicious recipes? Visit [VertexGPS.com](http://VertexGPS.com) for Delicious Dishes: recipe videos featuring our Case Managers. For more information on what Vertex GPS™: Guidance & Patient Support offers, see the next page.
Explore how Vertex GPS™: Guidance & Patient Support can help

Vertex GPS provides eligible patients with reimbursement support, potential financial resources, refill reminders, and ongoing product educational resources. Your dedicated Case Manager can provide support depending on your specific needs.

To find out more about Vertex GPS and the support resources available to you, including Delicious Dishes and Navigating Life With CF, visit www.VertexGPS.com.

If you are currently enrolled and want to learn more about how Vertex GPS can support you through your transition to SYMDEKO™ (tezacaftor/ivacaftor and ivacaftor), you can speak to your Case Manager at 1-877-752-5933 (press 2), Monday through Friday from 8:30 AM to 7:00 PM ET. If you have been prescribed SYMDEKO and are not enrolled, please speak with your healthcare provider.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Patient Information.