What is KALYDECO?

KALYDECO is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 12 months and older who have at least one mutation in their CF gene that is responsive to KALYDECO.

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

It is not known if KALYDECO is safe and effective in children under 12 months of age.

Please see Important Safety Information on pages 8-9 and full Prescribing Information for KALYDECO, including Patient Information.
KALYDECO is for the treatment of cystic fibrosis (CF) in people age 12 months and older who have one of the following 38 CF gene mutations:

- 2789+5G→A
- 3272-26A→G
- 3849+10kbC→T
- 711+3A→G
- A1067T
- A455E
- D110E
- D110H
- D1152H
- D1270N
- D579G
- E193K
- E56K
- E831X
- G1069R
- G1244E
- G178R
- G551D
- G551S
- G1069R
- G1244E
- G178R
- G551D
- G551S
- K1060T
- L206W
- P67L
- R1070W
- R1070Q
- S1251N
- S1255P
- S549N
- S549R
- S945L
- S977F
- S977F
- S977F
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- The following mutations were not included in the clinical studies but are predicted to respond based on results from a laboratory setting: A1067T, D110E, D110H, D1270N, E56K, E193K, F1052V, F1074L, G1069R, K1060T, R74W, and R1070Q
- F508del and 26 other mutations are not responsive to KALYDECO based on clinical and/or laboratory data

What is KALYDECO?

KALYDECO is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 12 months and older who have at least one mutation in their CF gene that is responsive to KALYDECO.

Talk to your doctor to learn if you have an indicated CF gene mutation. It is not known if KALYDECO is safe and effective in children under 12 months of age.
How does KALYDECO® (ivacaftor) work?

What is the underlying cause of cystic fibrosis (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.

How does KALYDECO® (ivacaftor) work?

KALYDECO works on a certain defect of the CFTR protein at the cellular level in people age 12 months and older with a KALYDECO responsive mutation.

The Cell of Someone With CF

KALYDECO helps the CFTR proteins stay open longer.

KALYDECO allows more chloride ions to pass into and out of the cells, helping to keep a balance of salt and water in certain organs, such as the lungs.

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

See how KALYDECO works
Watch the video at kalydeco.com/HowItWorks

Please see Important Safety Information on pages 8-9 and full Prescribing Information for KALYDECO, including Patient Information.
Who should not take KALYDECO?
Do not take KALYDECO if you take certain medicines or herbal supplements such as:
• the antibiotics rifampin (Rifamate®, Rifater®) or rifabutin (Mycobutin®)
• seizure medicines such as phenobarbital, carbamazepine (Tegretol®, Carbatrol®, and Equetro®), or phenytoin (Dilantin®, Phenytek®)
• St. John’s wort (Hypericum perforatum)
Talk to your doctor before taking KALYDECO if you take any of the medicines or supplements listed above.

What should I tell my doctor before taking KALYDECO?
Before you take KALYDECO, tell your doctor if you:
• have liver or kidney problems
• drink grapefruit juice, or eat grapefruit or Seville oranges
• are pregnant or plan to become pregnant. It is not known if KALYDECO will harm your unborn baby. You and your doctor should decide if you will take KALYDECO while you are pregnant
• are breastfeeding or planning to breastfeeding. It is not known if KALYDECO passes into your breast milk. You and your doctor should decide if you will take KALYDECO while you are breastfeeding

KALYDECO may affect the way other medicines work, and other medicines may affect how KALYDECO works.
Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements, as the dose of KALYDECO may need to be adjusted when taken with certain medications.
Especially tell your doctor if you take:
• antifungal medications such as ketoconazole (e.g., Nizoral®), itraconazole (e.g., Sporanox®), posaconazole (e.g., Noxafil®), 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 KALYDECO?
• KALYDECO 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 KALYDECO affects you
• You should avoid food containing grapefruit or Seville oranges while you are taking KALYDECO

What are the possible side effects of KALYDECO® (ivacaftor)?
KALYDECO can cause serious side effects.
High liver enzymes in the blood have been reported in patients receiving KALYDECO.
Your doctor will do blood tests to check your liver:
• before you start KALYDECO
• every 3 months during your first year of taking KALYDECO
• every year while you are taking KALYDECO
For patients who have had high liver enzymes in the past, the doctor may do blood tests to check the liver more often.
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 been noted in some children and adolescents receiving KALYDECO. Your doctor should perform eye examinations prior to and during treatment with KALYDECO to look for cataracts.
The most common side effects include:
• headache
• upper respiratory tract infection (common cold), including sore throat, nasal or sinus congestion, runny nose
• stomach (abdominal) pain
• diarrhea
• rash
• nausea
• dizziness
Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of KALYDECO. For more information, ask your doctor or pharmacist.
Call your doctor for medical advice about side effects. You are encouraged to report side effects to FDA at 1-800-FDA-1088.

Please see full Prescribing Information for KALYDECO, including Patient Information.
How was KALYDECO® (ivacaftor) studied?

The effect of KALYDECO on several different measures has been studied in the trials covered in the following pages.

- **Lung function (FEV₁)**
- **Sweat chloride levels**
- **Body mass index (BMI)**
- **CF respiratory symptoms**
- **Pulmonary exacerbations**

Lung function can be measured with an FEV₁ test, which measures how much air a person can exhale in a forced breath in 1 second.

Sweat chloride is a measure of the amount of salt in your sweat. People with cystic fibrosis (CF) have high levels of sweat chloride.

BMI is a measure of someone’s weight in relation to his or her height.

Respiratory symptoms are measured by the CFQ-R Respiratory Domain score, which is a tool used to measure respiratory symptoms, including coughing, mucus, and trouble breathing.

Pulmonary exacerbations are defined as changes in certain symptoms requiring changes in the use of oral, IV, or inhaled antibiotics.

Keep in mind that not all studies evaluated the same measures, and results shown on the following pages are an average of all people studied and differed among individuals and mutations. Your experience may be different.

A note for patients and caregivers

Keep in mind that not all mutations were evaluated in clinical studies, and those that were evaluated were not studied in all age groups. However, KALYDECO is approved for people age 1 year and older with any of the 38 indicated mutations on page 4. Talk to your healthcare provider to learn more about how these mutations were approved.

Review the results of studies of KALYDECO® (ivacaftor).

Click below to get the information you’re looking for.

- **Age 1 to less than 2 years old**
  - Study 8: G178R, G551D, S549N.

- **Age 2 to less than 6 years old**
  - Study 6: G551D, S549N.

- **Important Safety Information**
  - 16

- **Age 6 years and older**

- **Important Safety Information**
  - 24

- **Age 12 years and older**

*A KALYDECO is not indicated for people with CF who have the G970R mutation.

Please see Important Safety Information on pages 8-9 and full Prescribing Information for KALYDECO, including Patient Information.
**Study 8**

Study 8 was a 24-week study in which the safety of KALYDECO® (ivacaftor) was studied in 19 children age 1 to less than 2 years old with cystic fibrosis (CF). All patients enrolled took KALYDECO. No one in the study took placebo. Safety and tolerability were the main measures of this study.

**Mutations eligible for this study were:**


**Mutations included in this study:**

16 children had the G551D mutation, 2 had the S549N mutation, and 1 had the G178R mutation.

**How KALYDECO was given**

Children who weighed ~15 pounds (7 kg) to less than ~31 pounds (14 kg) received 50 mg of KALYDECO oral granules.

Children who weighed ~31 pounds (14 kg) or more received 75 mg of KALYDECO oral granules.

All children took KALYDECO oral granules mixed with 1 teaspoon of age-appropriate soft food or liquid every 12 hours with fat-containing food. All children continued to take their other CF treatments.

**Study results**

**Safety**

The type and frequency of side effects for children in the study were similar to those seen in KALYDECO® (ivacaftor) studies with people age 2 years and older. For safety information and side effects of KALYDECO, see pages 8-9.

**Sweat chloride**

Sweat chloride decreased

73.5 mmol/L on average

Sweat chloride is the amount of salt in your child’s sweat. A decrease in sweat chloride levels does not mean there will be an improvement in lung function (FEV).

KALYDECO was approved in people age 1 to less than 2 years old based on the benefits shown in studies of KALYDECO in older people as well as the safety assessment in this study.

Talk to your healthcare provider to learn more about how KALYDECO was approved in this age group.

Please see Important Safety Information on pages 8-9 and full Prescribing Information for KALYDECO, including Patient Information.
People with CF age 2 to less than 6 years old

Study 6

Study 6 was a 24-week study in which the safety of KALYDECO® (ivacaftor) was studied in 34 children age 2 to less than 6 years old with cystic fibrosis (CF). All children in this study took KALYDECO. No one in this study took placebo. Safety and tolerability were the main measures of this study.

Mutations eligible for this study were:

*KALYDECO is not indicated for people with CF who have the G970R mutation

Mutations included in this study:
32 children had the G551D mutation and 2 had the S549N mutation.

How KALYDECO was given

Children who weighed less than ~31 pounds (14 kg) received 50 mg of KALYDECO oral granules.

Children who weighed ~31 pounds (14 kg) or more received 75 mg of KALYDECO oral granules.

All children took KALYDECO oral granules mixed with 1 teaspoon of soft food or liquid every 12 hours with fat-containing food. All children continued to take their other CF treatments.

Study results

Safety

The type and frequency of side effects for children in the study were similar to those seen in KALYDECO® (ivacaftor) studies with people age 6 years and older. High liver enzymes were more common in children who had abnormal liver enzymes before starting KALYDECO.

For safety information and side effects of KALYDECO, see pages 8-9.

Sweat chloride

Sweat chloride decreased
45 mmol/L on average

Sweat chloride is the amount of salt in your child’s sweat. A decrease in sweat chloride levels does not mean there will be an improvement in lung function (FEV1).

KALYDECO was approved in people age 2 to less than 6 years old based on the benefits shown in studies of KALYDECO in older people as well as the safety assessment in this study.

Talk to your healthcare provider to learn more about how KALYDECO was approved in this age group.

Talk to your healthcare provider to learn more about how KALYDECO was approved in this age group.

Please see Important Safety Information on pages 8-9 and full Prescribing Information for KALYDECO, including Patient Information.
Who should not take KALYDECO?
Do not take KALYDECO if you take certain medicines or herbal supplements such as:
• the antibiotics rifampin (Rifamate®, Rifater®) or rifabutin (Mycobutin®)
• seizure medicines such as phenobarbital, carbamazepine (Tegretol®, Carbatrol®, and Equetro®),
or phenytoin (Dilantin®, Phenytek®)
• St. John’s wort (Hypericum perforatum)

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

What should I tell my doctor before taking KALYDECO?
Before you take KALYDECO, tell your doctor if you:
• have liver or kidney problems
• drink grapefruit juice, or eat grapefruit or Seville oranges
• are pregnant or plan to become pregnant. It is not known if KALYDECO will harm your unborn baby.
• are breastfeeding or planning to breastfeed. It is not known if KALYDECO passes into your breast milk.
• KALYDECO may affect the way other medicines work, and other medicines may affect how KALYDECO works.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements, as the dose of KALYDECO may need to be adjusted when taken with certain medications.

Especially tell your doctor if you take:
• antifungal medications such as ketoconazole (e.g., Nizoral®), itraconazole (e.g., Sporanox®),
posaconazole (e.g., Noxafil®), 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 KALYDECO?
• KALYDECO 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 KALYDECO affects you
• You should avoid food containing grapefruit or Seville oranges while you are taking KALYDECO

What are the possible side effects of KALYDECO® (ivacaftor)?
KALYDECO can cause serious side effects.

High liver enzymes in the blood have been reported in patients receiving KALYDECO.
Your doctor will do blood tests to check your liver:
• before you start KALYDECO
• every 3 months during your first year of taking KALYDECO
• every year while you are taking KALYDECO

For patients who have had high liver enzymes in the past, the doctor may do blood tests to check the liver more often.

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 been noted in some children and adolescents receiving KALYDECO. Your doctor should perform eye examinations prior to and during treatment with KALYDECO to look for cataracts.

The most common side effects include:
• headache
• upper respiratory tract infection (common cold), including sore throat, nasal or sinus congestion, runny nose
• stomach (abdominal) pain
• diarrhea
• rash
• nausea
• dizziness

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of KALYDECO. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You are encouraged to report side effects to FDA at 1-800-FDA-1088.

What is the Important Safety Information for KALYDECO® (ivacaftor)?

Please see full Prescribing Information for KALYDECO, including Patient Information.
Study 2

Study 2 was a 48-week study in which 52 people **age 6 to less than 12 years old** with a G551D mutation took KALYDECO® (ivacaftor [150 mg tablets]) or placebo with fat-containing food every 12 hours. Results were measured at different time points including 24 and 48 weeks. All people took their other cystic fibrosis (CF) treatments except for hypertonic saline through the entire length of the study (48 weeks). This study evaluated both the safety and possible benefits of KALYDECO.

**Mutation eligible and included in this study was:**

G551D.

**Study results**

<table>
<thead>
<tr>
<th>Lung function (FEV₁)</th>
<th>Lung function increased</th>
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<tr>
<td></td>
<td>12.5 percentage points greater average improvement, compared to placebo through 24 weeks.</td>
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<tr>
<td></td>
<td>10.0 percentage points greater average improvement, compared to placebo through 48 weeks.</td>
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Lung function was measured as FEV₁, or forced expiratory volume exhaled in 1 second.

**CF respiratory symptoms**

**No difference was seen in respiratory symptoms**

Compared to placebo through Week 48.

Respiratory symptoms are measured by the CFQ-R Respiratory Domain score, which is a tool used to measure respiratory symptoms, including coughing, mucus, and trouble breathing.

**Weight**

**Weight increased**

About 6 pounds (2.8 kg) on average, compared to placebo at Week 48.

**Sweat chloride**

**Sweat chloride decreased**

53 mmol/L on average, compared to placebo through Week 48.

Sweat chloride is the amount of salt in your sweat. A decrease in sweat chloride levels does not mean there will be an improvement in lung function (FEV₁).

KALYDECO® (ivacaftor) has also been studied in people age 12 and older who have the G551D mutation. Be sure to review the information on this study on pages 26-27.
People with CF age 6 years and older

In Study 4, 39 people age 6 and older who had an eligible cystic fibrosis (CF) mutation (listed below) took KALYDECO® (ivacaftor [150 mg tablets]) or placebo with fat-containing food every 12 hours. All people took all their other CF treatments except for hypertonic saline. Each person had an 8-week treatment period with KALYDECO and an 8-week treatment period with placebo. This study evaluated both the safety and possible benefits of KALYDECO.

Mutations eligible and included in this study were:
- G1244E
- G1349D
- G178R
- G551S
- G970R
- S1251N
- S1255P
- S549N
- S549R

*KALYDECO is not indicated for people with CF who have the G970R mutation.

Important considerations
- Results for the mutations studied varied by mutation. Not all mutations showed the same level of benefit when taking KALYDECO.
- Some people experienced less improvement compared to the average for all the people in the study. Others experienced more improvement.
- Talk to your healthcare provider to learn more about your specific mutation.

Study results

Lung function (FEV₁)

Lung function increased

In the overall population for the 9 mutations studied, people had a 10.7 percentage point average improvement in lung function compared to placebo, from the start of the study through Week 8.

Results varied by mutation.

Sweat chloride

Sweat chloride decreased

In the overall population for the 9 mutations studied, people had a 50 mmol/L average decrease in sweat chloride compared to placebo from the start of the study through Week 8.

Results varied by mutation.

Body mass index (BMI)

BMI increased

In the overall population for the 9 mutations studied, people had a 0.66 kg/m² on average increase in BMI compared to placebo at Week 8.

Results varied by mutation.

CF respiratory symptoms

CF respiratory symptoms improved

In the overall population for the 9 mutations studied, people had a 9.6 point average improvement in CF respiratory symptoms compared to placebo, from the start of the study through Week 8.

Results varied by mutation.

Sweat chloride is the amount of salt in your sweat. A decrease in sweat chloride levels does not mean there will be an improvement in lung function (FEV₁).
People with CF age 6 years and older

Study 5

Study 5 was a 24-week study in which 69 people age 6 and older with an R117H mutation took either KALYDECO® (ivacaftor [150 mg tablets]) or placebo with fat-containing food every 12 hours, along with their other cystic fibrosis (CF) treatments. This study evaluated both the safety and possible benefits of KALYDECO.

Mutation eligible and included in this study was:
R117H.

What was studied?

Lung function (FEV1) was the main measure of this study

Lung function was measured as FEV1, or forced expiratory volume exhaled in 1 second.

Sweat chloride

CF respiratory symptoms (cough, mucus, and trouble breathing)

Body mass index (BMI)

Pulmonary exacerbations

Safety

Some people in this study showed improvement in these measures, but others did not.

- Please talk to your healthcare provider if you’d like to learn about the results of this study

Please see Important Safety Information on pages 8-9 and full Prescribing Information for KALYDECO, including Patient Information.
Who should not take KALYDECO?
Do not take KALYDECO if you take certain medicines or herbal supplements such as:
• the antibiotics rifampin (Rifamate®, Rifater®) or rifabutin (Mycobutin®)
• seizure medicines such as phenobarbital, carbamazepine (Tegretol®, Carbatrol®, and Equetro®), or phenytoin (Dilantin®, Phenytek®)
• St. John’s wort (Hypericum perforatum)

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

What should I tell my doctor before taking KALYDECO?
Before you take KALYDECO, tell your doctor if you:
• have liver or kidney problems
• drink grapefruit juice, or eat grapefruit or Seville oranges
• are pregnant or plan to become pregnant. It is not known if KALYDECO will harm your unborn baby. You and your doctor should decide if you will take KALYDECO while you are pregnant
• are breastfeeding or planning to breastfeed. It is not known if KALYDECO passes into your breast milk. You and your doctor should decide if you will take KALYDECO while you are breastfeeding

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

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements, as the dose of KALYDECO may need to be adjusted when taken with certain medications.

Especially tell your doctor if you take:
• antifungal medications 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 KALYDECO?
• KALYDECO 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 KALYDECO affects you
• You should avoid food containing grapefruit or Seville oranges while you are taking KALYDECO

What are the possible side effects of KALYDECO® (ivacaftor)?
KALYDECO can cause serious side effects.

High liver enzymes in the blood have been reported in patients receiving KALYDECO.
Your doctor will do blood tests to check your liver:
• before you start KALYDECO
• every 3 months during your first year of taking KALYDECO
• every year while you are taking KALYDECO

For patients who have had high liver enzymes in the past, the doctor may do blood tests to check the liver more often.

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 been noted in some children and adolescents receiving KALYDECO. Your doctor should perform eye examinations prior to and during treatment with KALYDECO to look for cataracts.

The most common side effects include:
• headache
• upper respiratory tract infection (common cold), including sore throat, nasal or sinus congestion, runny nose
• stomach (abdominal) pain
• diarrhea
• rash
• nausea
• dizziness

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of KALYDECO. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You are encouraged to report side effects to FDA at 1-800-FDA-1088.
Study 1

Study 1 was a 48-week study in which 161 people age 12 and older with a G551D mutation took KALYDECO® (ivacaftor [150 mg tablets]) or placebo. Results were measured at different time points including 24 and 48 weeks. All people took all their other cystic fibrosis (CF) treatments except for hypertonic saline throughout the entire length of the study (48 weeks). This study evaluated both the safety and possible benefits of KALYDECO.

Mutation eligible and included in this study was:

G551D.

Study results

Lung function (FEV₁)

Lung function increased

10.6 percentage points greater average improvement, compared to placebo through 24 weeks.
10.5 percentage points greater average improvement, compared to placebo through 48 weeks.

Lung function was measured as FEV₁, or forced expiratory volume exhaled in 1 second.

CF respiratory symptoms

CF respiratory symptoms improved

8.6 points on average compared to placebo, from the start of the study through Week 48.

Respiratory symptoms are measured by the CFQ-R Respiratory Domain score, which is a tool used to measure respiratory symptoms, including coughing, mucus, and trouble breathing.

Pulmonary exacerbations

Pulmonary exacerbations decreased

Nearly 7 out of 10 people who took KALYDECO® (ivacaftor) did not have a pulmonary exacerbation, compared to around 4 out of 10 people who took placebo at Week 48.

Pulmonary exacerbations are defined as changes in certain symptoms requiring changes in the use of oral, IV, or inhaled antibiotics.

Weight

Weight increased

About 6 pounds (2.7 kg) on average, compared to placebo at Week 48.

Sweat chloride

Sweat chloride decreased

48 mmol/L on average, compared to placebo at Week 48.

Sweat chloride is the amount of salt in your sweat. A decrease in sweat chloride levels does not mean there will be an improvement in lung function (FEV₁).
Study 7

Study 7 was an 8-week study in which people **age 12 and older** with 1 copy of the F508del mutation and a second mutation predicted to respond to KALYDECO® (ivacaftor) took either KALYDECO (150 mg tablets) or placebo with fat-containing food every 12 hours. All people took all their other cystic fibrosis (CF) treatments except for hypertonic saline. This study evaluated both the safety and possible benefits of KALYDECO.

In this study, 156 people took KALYDECO (150 mg tablet) and 161 people took placebo.

**Mutations eligible and included in this study were:**


**Important considerations**

- Lung function and respiratory results varied by mutation. Not all mutations showed the same level of benefit when taking KALYDECO.
- Some people experienced less improvement compared to the average for all the people in the study. Others experienced more improvement.
- This is not intended to represent the full study design or results.
- Talk to your healthcare provider for more information.

**Study results**

**Lung function (FEV1)**

- *Lung function increased* 4.7 percentage points on average in the overall population studied compared to placebo, from the start of the study to the average of Week 4 and Week 8. **Results varied by mutation.**

Lung function was measured as FEV1, or forced expiratory volume exhaled in 1 second.

**CF respiratory symptoms improved**

- *CF respiratory symptoms improved* 9.7 points on average in the overall population studied compared to placebo, from the start of the study to the average of Week 4 and Week 8. **Results varied by mutation.**

Respiratory symptoms are measured by the CFQ-R Respiratory Domain score, which is a tool used to measure respiratory symptoms, including coughing, mucus, and trouble breathing.
Taking KALYDECO oral granules and tablets

KALYDECO oral granules are prescribed based on weight for people age 1 to less than 6 years old and come in 2 different strengths.

<table>
<thead>
<tr>
<th>WEIGHT-BASED DOSE</th>
<th>EACH DOSE</th>
<th>TOTAL DAILY DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>~15 pounds to less than 31 pounds (7 kg to 14 kg)</td>
<td>50-mg packet (1 packet every 12 hours)</td>
<td>100 mg (2 packets per day)</td>
</tr>
<tr>
<td>~31 pounds or more (14 kg or more)</td>
<td>75-mg packet (1 packet every 12 hours)</td>
<td>150 mg (2 packets per day)</td>
</tr>
</tbody>
</table>

KALYDECO is supplied as tablets for people 6 years and older.

<table>
<thead>
<tr>
<th>EACH DOSE</th>
<th>TOTAL DAILY DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>150-mg tablet (1 tablet every 12 hours)</td>
<td>300 mg (2 tablets per day)</td>
</tr>
</tbody>
</table>

How to give your child KALYDECO oral granules

- Hold 1 packet of KALYDECO oral granules with the cut line on top
- Shake the packet gently to settle the KALYDECO granules
- Tear or cut the packet open along the cut line
- Carefully pour all of the KALYDECO granules into 1 teaspoon (5 mL) of soft food or liquid such as applesauce, or other pureed fruits or vegetables, yogurt, water, milk, or juice
  - Food or liquid should be at or below room temperature
  - Then, mix the granules with the 1 teaspoon of food or liquid

How should KALYDECO® (ivacaftor) be taken?

- Make sure to eat fat-containing food just before or after the dose of KALYDECO granules. This helps the body absorb KALYDECO better
- Examples of fat-containing food include:
  - Eggs
  - Peanut butter
  - Whole-milk cheese
  - Whole-milk yogurt
- Your doctor can help you choose healthy fat-containing meals and snacks

See page 34 for some fat-containing foods you can consider when taking KALYDECO.

Always take KALYDECO® (ivacaftor) tablets and oral granules with fat-containing food

Preparation

- Hold 1 packet of KALYDECO oral granules with the cut line on top
- Shake the packet gently to settle the KALYDECO granules
- Tear or cut the packet open along the cut line
- Carefully pour all of the KALYDECO granules into 1 teaspoon (5 mL) of soft food or liquid such as applesauce, or other pureed fruits or vegetables, yogurt, water, milk, or juice
  - Food or liquid should be at or below room temperature
  - Then, mix the granules with the 1 teaspoon of food or liquid

Administration

- Within 1 hour of mixing, give KALYDECO to your child
- Make sure the entire medicine mixture is taken

Learn additional important information about how to take KALYDECO oral granules and tablets on the next page.
How should KALYDECO® (ivacaftor) be taken? (Cont.)

Taking KALYDECO oral granules and tablets
Avoid foods or drinks that contain grapefruit or Seville oranges, as these may affect the amount of KALYDECO in the body.

Take KALYDECO, plus all your other cystic fibrosis (CF) therapies, exactly as your healthcare provider tells you to take them

Be sure to talk to your or your child’s healthcare provider before starting, changing, or stopping any CF therapies or other medications, including prescription and non-prescription medicines, vitamins, and herbal supplements.

What to do if a dose of KALYDECO is missed
If you or your child miss a dose of KALYDECO and it is within 6 hours of when you usually take it, take the dose of KALYDECO as prescribed with fat-containing food as soon as possible.

If you or your child miss a dose and it is more than 6 hours after the time you usually take it, skip that dose only and take the next dose with fat-containing food when you usually take it. Do not take 2 doses at the same time to make up for a missed dose.
Here are some breakfast, snack, and dinner ideas that you can consider when taking KALYDECO.

<table>
<thead>
<tr>
<th>MEAL</th>
<th>IF YOU HAVE TIME</th>
<th>IF YOU’RE IN A RUSH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>• Scrambled eggs with avocado on multigrain toast</td>
<td>• Granola with whole milk</td>
</tr>
<tr>
<td></td>
<td>• Chocolate chip pancakes</td>
<td>• Bagel with peanut butter</td>
</tr>
<tr>
<td></td>
<td>• Grilled peanut butter and banana sandwich</td>
<td></td>
</tr>
<tr>
<td>Snack</td>
<td>• Peach shake</td>
<td>• Trail mix</td>
</tr>
<tr>
<td></td>
<td>• Cream cheese fruit dip</td>
<td>• Whole-milk string cheese</td>
</tr>
<tr>
<td></td>
<td>• Chocolate pudding</td>
<td>• High-fat hummus and celery sticks</td>
</tr>
<tr>
<td>Dinner</td>
<td>• Baked chicken nuggets</td>
<td>• Caesar salad with chicken and</td>
</tr>
<tr>
<td></td>
<td>• Simple mac and cheese</td>
<td>Parmesan cheese</td>
</tr>
<tr>
<td></td>
<td>• Sloppy Joes</td>
<td>• Sausage pizza</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Grilled cheese sandwich</td>
</tr>
</tbody>
</table>

Looking for new and delicious recipes?
Visit VertexGPS.com for Delicious Dishes: recipe videos featuring our very own Case Managers. For more information on Vertex GPS℠: Guidance & Patient Support, see the next page.
Explore how Vertex GPS™: Guidance and Patient Support can help

Vertex GPS provides eligible patients with reimbursement support, information about financial resources, refill reminders, and ongoing educational materials.

If you are currently enrolled and want to learn more about how GPS can support you, 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 KALYDECO® (ivacaftor) and are not enrolled, please speak with your healthcare provider.

To find out more about GPS and the support resources available to you, including Delicious Dishes, visit VertexGPS.com.

Please see full Prescribing Information for KALYDECO, including Patient Information.