

Kalydeco[®] (ivacaftor) – Expanded indication

- On August 1, 2017, [Vertex announced](#) the FDA approval of [Kalydeco \(ivacaftor\)](#) for use in more than 600 patients ≥ 2 years of age with cystic fibrosis (CF) who have one of five residual function mutations that result in a splicing defect in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.
 - This expands the use of Kalydeco to include patients who have one of 38 ivacaftor-responsive mutations in the CFTR gene.
 - Previously, Kalydeco was approved in patients with one of 23 residual function mutations in the CFTR gene.
- Kalydeco is indicated for the treatment of CF in ≥ 2 years old who have the CFTR gene that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data.

- Mutations that are responsive to Kalydeco are listed in the following table:

<i>E56K</i>	<i>G178R</i>	<i>S549R</i>	<i>S977F</i>	<i>F1074L</i>	<i>2789+5G→A*</i>
<i>P67L</i>	<i>E193K</i>	<i>G551D</i>	<i>F1052V</i>	<i>D1152H</i>	<i>3272-26A→G*</i>
<i>R74W</i>	<i>L206W</i>	<i>G551S</i>	<i>K1060T</i>	<i>G1244E</i>	<i>3849+10kbC→T*</i>
<i>D110E</i>	<i>R347H</i>	<i>D579G</i>	<i>A1067T</i>	<i>S1251N</i>	
<i>D110H</i>	<i>R352Q</i>	<i>711+3A→G*</i>	<i>G1069R</i>	<i>S1255P</i>	
<i>R117C</i>	<i>A455E</i>	<i>E831X*</i>	<i>R1070Q</i>	<i>D1270N</i>	
<i>R117H</i>	<i>S549N</i>	<i>S945L</i>	<i>R1070W</i>	<i>G1349D</i>	

*Mutations that are part of the expanded indication.

- The expanded approval for Kalydeco was based on a placebo-controlled trial in 246 patients with CF who were heterozygous for the F508del mutation with a second mutation predicted to be responsive to ivacaftor. The primary efficacy endpoint was the mean absolute change from baseline in percent predicted forced expiratory volume in 1 second (ppFEV₁) averaged at weeks 4 and 8.
 - For the overall population, treatment with ivacaftor compared to placebo resulted in significant improvement in ppFEV₁ (4.7 percent points from baseline, $p < 0.0001$)
 - Statistically significant improvements compared to placebo were also observed in the subgroup of patients with splice mutations and missense mutations.
- For adults and pediatric patients ≥ 6 years of age, the recommended dose of Kalydeco is one 150 mg tablet orally every 12 hours with fat-containing food.
- For patients ages 2 to less than 6 years old, the recommended dose of Kalydeco (oral granules) is based on weight. See table below.

Body Weight	Dose	Total Daily Dose
< 14 kg	one 50 mg packet every 12 hours	100 mg/day
≥ 14 kg	one 75 mg packet every 12 hours	150 mg/day

- The entire contents of each packet of oral granules should be mixed with 5 mL (one teaspoon) of age-appropriate soft food or liquid and completely consumed.

- The safety and efficacy of Kalydeco for patients < 2 years old has not been established. The use of Kalydeco in children < 2 years of age is not recommended.



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