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:

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

*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 ($ppFEV_1$) 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.

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— 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.