Kalydeco® (ivacaftor) – Expanded indication

- On May 17, 2017, the FDA announced the approval of Vertex's Kalydeco (ivacaftor) for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to ivacaftor potentiation based on clinical and/or *in vitro* assay data.
    - This approval triples the number of rare gene mutations that the drug can now treat, expanding the indication from the treatment of 10 mutations, to 33.
    - If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

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

*E56K**	*G178R*	*S549R*	*K1060T**	*G1244E*	*P67L**	*E193K**	*G551D*
*A1067T**	*S1251N*	*R74W**	*L206W**	*G551S*	*G1069R**	*S1255P*	*D110E**
*R347H**	*D579G**	*R1070Q**	*D1270N**	*D110H**	*R352Q**	*S945L**	*R1070W**
G1349D	*R117C**	*A455E**	*S977F**	*F1074L**	*R117H*	*S549N*	*F1052V**
*D1152H**							

*Mutations that are part of the expanded indication.

- CF is caused by a defective or missing CFTR protein resulting from mutations in the CFTR gene. The defective CFTR gene cannot regulate the movement of chloride and water, causing mucus, sweat and digestive secretions to become sticky and thick. The secretions build up in the lungs, digestive tract and other parts of the body leading to severe respiratory and digestive problems, as well as other complications such as infections and diabetes.

- CF affects about 30,000 people in the U.S. The expanded indication will affect another 3% of the CF population, impacting approximately 900 patients.

- The expanded indication for Kalydeco was approved based on clinical data from numerous prior studies and a demonstrated *in vitro* response employing a well-established, analytically validated method.
    - The additional CFTR mutations produce CFTR protein at the cell surface and have shown *in vitro* increases in chloride transport in response to Kalydeco by at least 10% of normal over baseline.

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- The recommended dose of Kalydeco for adults and pediatric patients age 6 years and older is one 150 mg tablet taken orally every 12 hours with fat-containing food.
    - The dose of Kalydeco for pediatric patients 2 to less than 6 years of age is weight based. Refer to the Kalydeco drug label for dosing information.