



State of California—Health and Human Services Agency
Department of Health Care Services



Edmond G. Brown Jr
Governor

DATE: April 15, 2015

N.L.: 03-0415
Supersedes N L: 10-0514

TO: ALL COUNTY CALIFORNIA CHILDREN SERVICES (CCS) PROGRAM
ADMINISTRATORS, MEDICAL CONSULTANTS, STATE SYSTEMS OF
CARE DIVISION STAFF AND GENETICALLY HANDICAPPED PERSONS
PROGRAM (GHPP)

SUBJECT: IVACAFTOR (KALYDECO™)-EXPANDED INDICATION FOR USE AND
MINIMUM AGE

I. PURPOSE

The purpose of this updated Numbered Letter (N.L.) is to modify the CCS Program and GHPP policy regarding the authorization of ivacaftor, as a treatment for cystic fibrosis (CF) due to gating mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) genes. Ivacaftor is the first of a new class of drugs known as CFTR potentiators, and has been associated with significant clinical improvement in individuals that have a CFTR gating mutation in at least one allele. Previous indications for ivacaftor were gating mutations G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, and S549R, and treatment at six years of age or older. The indication for ivacaftor has now been expanded to include mutation R117H, and with the lowering of minimum age to two years.

II. BACKGROUND

Cystic fibrosis is a life-threatening autosomal recessive genetic disease affecting respiratory and digestive systems. In California, CF is found in all race/ethnic groups at a prevalence of around 1/3500 in non-Hispanic whites, 1/7900 in Hispanic whites, 1/8000 in non-Hispanic blacks, and 1/23,500 in Asians and others. CF is caused by a defective gene for the CFTR. A defective CFTR results in decreased secretion of chloride and increased reabsorption of sodium and water across epithelial cells. This leads to viscous (sticky) secretions, which are harder to clear and increase susceptibility to life-threatening pulmonary infections. In addition, the viscous secretions obstruct the process of digestion, leading to malabsorption of food.

Standard therapies for CF target amelioration of symptoms and prevention of infection. Ivacaftor, on the other hand, targets the pathology of the disease. In individuals with one of the CFTR gating mutations listed above (2-5 percent of those with CF), ivacaftor binds to the defective receptor, and facilitates passage of chloride ions across the defective CFTR, normalizing the secretions. Ivacaftor efficacy for the G551D mutation over a 48-week period was demonstrated in a Phase III trial of individuals 12 years and older, in which there were 55 percent fewer exacerbations, pulmonary lung function scores (FEV1) improvement by an average of 10 percent, and better quality of life. Additional trials extending this study to 60 weeks, and with children ages 6-11, found sustained improvement in lung function. On January 31, 2012, Food and Drug Administration (FDA) approved ivacaftor for use in persons age six and over with CF who have the G551D mutation. The recommended dose is 150mg every 12 hours for adult and pediatric (six years and older) patients.

In February 2014, ivacaftor was approved by the FDA for expanded use for G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R mutations (occurring in less than 1 percent of CF patients), based on an 8-week Phase III clinical trial showing improvement in lung function as determined by the mean absolute change from baseline FEV1.

In March 2015, the FDA approved use for patients with the R117H mutation, and lowered the age limit to two years.

III. POLICY

Effective the date of this letter, ivacaftor is a CCS/GHPP benefit when:

- A. Prescribed by a CCS/GHPP-approved pulmonology special care center physician, and;
- B. For a CCS/GHPP client with CF and a CFTR gating mutation in at least one allele (Gating mutations include G1244E, G1349D, G178R, G551D, G551S, S1251N, S1255P, S549N, S549R, and R117H.), whose care is under the supervision and monitoring of a CCS/GHPP approved Cystic Fibrosis and Pulmonology Center, and;
- C. For a client two years of age or older, and;

- D. Request is submitted with documentation of pulmonary function testing abnormalities; poor weight gain, poor nutritional status, or growth; and/or symptom record.

IV. POLICY IMPLEMENTATION

- A. Ivacaftor (Kalydeco™) requires separate authorization.
- B. All requests shall be reviewed by a CCS Program County Medical Director or designee before authorization of ivacaftor.
- C. Initial Authorization:
 - 1. Shall be for a 60-day trial.
 - 2. Prior to authorization, documentation must be submitted showing positive genetic test for G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R or R117H in the CFTR gene, using a testing method that can detect the mutation.
- D. Extension of the initial authorization shall be granted when:
 - 1. Documentation is submitted by the CCS/GHPP approved pulmonary special care center demonstrating at least one of the following after 60 days of ivacaftor:
 - a. Improvement in FEV1 from baseline by at least five percent.
 - b. Reduction in sweat chloride from baseline by at least 20mEq/L.
 - c. Improvement in Symptom Record from baseline.
 - d. Appropriate weight gain/improvement in nutritional status.
 - 2. For a six-month period or until program eligibility end date, whichever is shorter.

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E. The following shall be considered when reviewing requests for ivacaftor:

1. Ivacaftor is not effective in individuals with two copies of the F508del CFTR mutation (i.e., F508del/F508del).
2. Ivacaftor is not a replacement for conventional adjunctive therapy.
3. At this time, the manufacturer recommends not crushing or splitting the tablets. The tablets should be swallowed whole.

F. Exceptions will be reviewed on a case-by-case basis by State Systems of Care Division (SCD) Medical Director or designee.

If you have any questions regarding this N.L., please contact Marcia Ehinger, M.D. via e-mail at Marcia.Ehinger@dhcs.ca.gov or Jill Abramson, M.D, Chief, Medical Policy & Consultation Section, via e-mail at Jill.Abramson@dhcs.ca.gov.

Sincerely,

ORIGINAL SIGNED BY ROBERT J. DIMAND

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Chief Medical Officer
California Children's Services
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