Criteria Based Consultation Prescribing Program

CRITERIA FOR DRUG COVERAGE
ivacaftor (Kalydeco®)

**Initial approval criteria:** Non-formulary ivacaftor (Kalydeco®) will be covered on the prescription drug benefit for 12 months when the following criteria are met:

- Prescriber specializes in the treatment of cystic fibrosis
- Patient is at least 12 months of age
- Patient is NOT homozygous for the F508del mutation in the CFTR gene
- At least one of the following mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene:

<table>
<thead>
<tr>
<th>Mutation</th>
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<tbody>
<tr>
<td>P67L</td>
<td>R117C</td>
<td>R347H</td>
<td>S549R</td>
<td>E831X</td>
<td>K1060T</td>
<td>R1070W</td>
<td>S1251N</td>
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<tr>
<td>R74W</td>
<td>G178R</td>
<td>R352Q</td>
<td>G551D</td>
<td>S945L</td>
<td>A1067T</td>
<td>F1074L</td>
<td>S1255P</td>
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<tr>
<td>D110E</td>
<td>E193K</td>
<td>A455E</td>
<td>G551S</td>
<td>S977F</td>
<td>G1069R</td>
<td>D1152H</td>
<td>D1270N</td>
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<tr>
<td>D110H</td>
<td>L206W</td>
<td>S549N</td>
<td>D579G</td>
<td>F1052V</td>
<td>R1070Q</td>
<td>G1244E</td>
<td>G1349D</td>
</tr>
<tr>
<td>2789+5G→A</td>
<td>3272-26A→G</td>
<td>3849+10kbC→T</td>
<td>E56K</td>
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- Patients with a R117H mutation in the CFTR gene who have clinically significant disease (patients with R117H and the 5T form of the poly-T tract, but not 7T or 9T)

**Continued use criteria:** Non-formulary ivacaftor (Kalydeco®) will continue to be covered on the prescription drug benefit for 12 months when the following criteria are met:

- Patient is adherent to therapy regimen as evidenced by refill history and clinic visits.
- AST, ALT, bilirubin, and ophthalmic changes\(^\) are monitored at least annually
- If 6+ years of age: a clinically meaningful response to therapy as evidenced by at least one of the following:
  1. Improved or stabilized percent predicted FEV\(_1\)
  2. Peds and adolescents: BMI increased or stabilized within growth curve percentile
  3. Adults: weight increased or stabilized
  4. Decreased exacerbations and/or hospitalizations (pulmonary related)
  5. Prescriber attests that the patient has a clinically meaningful response to therapy

\(^\) Changes in the following liver enzymes should be reviewed within 12 months after discontinuation of ivacaftor:

- AST
- ALT
- Bilirubin

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Notes:

If the patient's genotype is unknown, an FDA-approved 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.

Transaminases (ALT and AST) should be assessed at baseline, every 3 months for one year, and annually thereafter. Increased monitoring may be necessary in patients with a history of elevated ALT, AST, or bilirubin.

^ Patients up to 17 years of age: Ophthalmic examination recommended prior to initiation of therapy and at follow-up intervals.

Strong inducers of CYP3A inducers reduce exposure of ivacaftor, which may diminish its effectiveness; therefore, co-administration is not recommended.