Criteria Based Consultation Prescribing Program

CRITERIA FOR DRUG COVERAGE

**tezacaftor-ivacaftor; ivacaftor (Symdeko)**

Non-formulary **tezacaftor-ivacaftor; ivacaftor (Symdeko)** 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 (CF)
- Patient is at least 6 years of age
- Diagnosis of CF confirmed by FDA-cleared mutation test or CLIA certified laboratory.
- Two copies of F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene -OR-
- One of the following mutations known to be responsive to tezacaftor-ivacaftor; ivacaftor in the CFTR gene

<table>
<thead>
<tr>
<th>Mutation</th>
<th>A1067T</th>
<th>D1270N</th>
<th>E56K</th>
<th>K1060T</th>
<th>R117C</th>
<th>S945L</th>
<th>2789+5G→A</th>
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</thead>
<tbody>
<tr>
<td>A455E</td>
<td>D110E</td>
<td>E831X</td>
<td>L206W</td>
<td>R347H</td>
<td>S977F</td>
<td>3272-26A→G</td>
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<tr>
<td>D110H</td>
<td>D579G</td>
<td>F1052V</td>
<td>P67L</td>
<td>R352Q</td>
<td></td>
<td>3849+10kbC→T</td>
<td></td>
</tr>
<tr>
<td>D1152H</td>
<td>E193K</td>
<td>F1074L</td>
<td>R1070W</td>
<td>R74W</td>
<td></td>
<td>711+3A→G</td>
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</tr>
</tbody>
</table>

**Continued Use Criteria**: Non-formulary **tezacaftor-ivacaftor; ivacaftor (Symdeko)** 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\(^\wedge\) are monitored at least annually
- Clinically meaningful response to therapy as evidenced by at least one of the following:
  1. Improved or stabilized percent predicted FEV\(1\)
  2. Adolescents: BMI increased or stabilized within growth curve percentile
  3. Adults: Bodyweight increased or stabilized
  4. Decreased exacerbations and/or hospitalizations (pulmonary related)
  5. Prescriber attests that the patient has a clinically meaningful response to therapy

\(^\wedge\) Symptoms that may suggest cholestasis include: jaundice, dark urine, light-colored stools, itching, abdominal pain, and fatigue.
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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.