GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA, SEE BELOW)

1. Does the patient have a diagnosis of cystic fibrosis (CF) and is homozygous for the F508del-CFTR gene mutation (as documented by copy of lab report)?
   
   If yes, continue to #3.
   If no, continue to #2.

2. Does the patient have a diagnosis of cystic fibrosis (CF) and has at least one of the following mutations in the CFTR gene (as documented by copy of lab report)?

<table>
<thead>
<tr>
<th>Mutation 1</th>
<th>Mutation 2</th>
<th>Mutation 3</th>
<th>Mutation 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>2789+5G→A</td>
<td>D110E</td>
<td>E56K</td>
<td>P67L</td>
</tr>
<tr>
<td>3272-26A→G</td>
<td>D110H</td>
<td>E831X</td>
<td>R1070W</td>
</tr>
<tr>
<td>3849+10kbC→T</td>
<td>D1152H</td>
<td>F1052V</td>
<td>R117C</td>
</tr>
<tr>
<td>711+3A→G</td>
<td>D1270N</td>
<td>F1074L</td>
<td>R347H</td>
</tr>
<tr>
<td>A1067T</td>
<td>D579G</td>
<td>K1060T</td>
<td>R352Q</td>
</tr>
<tr>
<td>A455E</td>
<td>E193K</td>
<td>L206W</td>
<td>R74W</td>
</tr>
</tbody>
</table>

   If yes, continue to #3.
   If no, do not approve.

DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE
TEZACAFTOR/IVACAFTOR

INITIAL CRITERIA (CONTINUED)

3. Does the patient meet **ALL** of the following criteria?
   - The patient is 12 years of age or older
   - Therapy is prescribed by or in consultation with a pulmonologist or cystic fibrosis (CF) expert
   - Stable disease as defined by previous or current treatment with another agent used in the treatment of cystic fibrosis (CF) (e.g., oral/inhaled corticosteroid, bronchodilator, inhaled antibiotics, dornase alfa, or acetylcysteine)
   - Baseline FEV1 (forced expiratory volume in one second) at least 40% or higher (as documented by lab report or chart notes)
   - The patient is not on concurrent therapy with other ivacaftor-containing products (e.g., Kalydeco, Orkambi)
   - The patient is not currently pregnant

If yes, approve for 24 weeks by HICL with a quantity limit of #2 tablets per day.

**APPROVAL TEXT:** Renewal requires **ALL** of the following criteria (as documented by lab report or chart notes):
   - The patient has demonstrated **ONE** of the following:
     - Maintenance or improvement in FEV1 (forced expiratory volume in 1 second)
     - Maintenance or improvement in BMI (body mass index)
     - Reduction in pulmonary exacerbations
   - The patient is not currently pregnant

If no, do not approve.

**INITIAL DENIAL TEXT:** The guideline named **TEZACAFTOR/IVACAFTOR** (Symdeko) requires a diagnosis of cystic fibrosis. In addition, the following criteria must also be met:
   - The patient is homozygous for the F508del-CFTR gene mutation (as documented by copy of lab report) OR has one of the following mutations in the CFTR gene (as documented by copy of lab report)

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

   - The patient is 12 years of age or older
   - Therapy is prescribed by or in consultation with a pulmonologist or CF expert
   - Stable disease as defined by previous or current treatment with another agent used in the treatment of cystic fibrosis (CF) (e.g., oral/inhaled corticosteroid, bronchodilator, inhaled antibiotics, dornase alfa, or acetylcysteine)

*Initial denial text continued on next page*
TEZACAFTOR/IVACAFTOR

INITIAL CRITERIA (CONTINUED)

- Baseline FEV1 (forced expiratory volume in one second) at least 40% or higher (as documented by lab report or chart notes)
- The patient is not on concurrent therapy with other ivacaftor-containing products (e.g., Kalydeco, Orkambi)
- The patient is not currently pregnant

RENEWAL CRITERIA

1. Does the patient have a diagnosis of cystic fibrosis (CF) and meet ALL of the following criteria (as documented by lab report or chart notes)?
   - The patient has demonstrated ONE of the following:
     - Maintenance or improvement in FEV1 (forced expiratory volume in 1 second)
     - Maintenance or improvement in BMI (body mass index)
     - Reduction in pulmonary exacerbations
   - Patient is not currently pregnant

   If yes, approve for 12 months by HICL with a quantity limit of #2 tablets per day.
   If no, do not approve.

RENEWAL DENIAL TEXT: The guideline named TEZACAFTOR/IVACAFTOR (Symdeko) requires a diagnosis of cystic fibrosis (CF) for renewal. In addition, the following criteria must also be met:
   - The patient has demonstrated ONE of the following (as documented by lab report or chart notes):
     - Maintenance or improvement in FEV1 (forced expiratory volume in 1 second)
     - Maintenance or improvement in BMI (body mass index)
     - Reduction in pulmonary exacerbations
   - Patient is not currently pregnant

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Symdeko (tezacaftor-ivacaftor).

REFERENCES

Created: 02/18
Effective: 06/01/19