PRIOR AUTHORIZATION POLICY

POLICY: Cystic Fibrosis – Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets – Vertex)

TAC APPROVAL DATE: 03/06/2019; selected revision 06/26/2019

OVERVIEW
Symdeko is indicated for the treatment of patients ≥ 6 years of age with cystic fibrosis (CF) who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.1 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. Table 1 lists responsive CFTR mutations based on: 1) a clinical forced expiratory volume in 1 second (FEV1) response and/or 2) in vitro data in FRT cells, indicating that tezacaftor/ivacaftor increases chloride transport to ≥10% of untreated normal over baseline. CFTR gene mutations that are not responsive to ivacaftor alone (Kalydeco®) are not expected to respond to Symdeko except for F508del homozygotes.

Table 1. List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Symdeko.1

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Response to Symdeko</th>
</tr>
</thead>
<tbody>
<tr>
<td>E56K</td>
<td>E193K</td>
</tr>
<tr>
<td>P67L</td>
<td>L206W</td>
</tr>
<tr>
<td>R74W</td>
<td>R347H</td>
</tr>
<tr>
<td>D110E</td>
<td>R352Q</td>
</tr>
<tr>
<td>D110H</td>
<td>A455E</td>
</tr>
<tr>
<td>R117C</td>
<td>D579G</td>
</tr>
<tr>
<td>F508del</td>
<td>711+3A ⇒ G</td>
</tr>
</tbody>
</table>

Table 1. List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Symdeko.1

Guidelines
Guidelines from the CF Foundation (2018) provide guidance on the use of CFTR therapy in patients with CF; Symdeko is not addressed.4

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Symdeko. Because of the specialized skills required for evaluation and diagnosis of patients treated with Symdeko as well as the monitoring required for adverse events and efficacy, approval requires Symdeko to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 3 years unless otherwise noted below.

Automation: None

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Symdeko is recommended in those who meet the following criteria:
FDA-Approved Indications

1. **Cystic Fibrosis (CF).** Approve Symdeko for 3 years in patients who meet the following criteria A, B, **AND** C:
   
   A) The patient meets **ONE** of the following conditions (i or ii):
      
      
      ii. The patient has two copies of the F508del mutation; **AND**
      
   B) The patient is ≥ 6 years of age; **AND**
      
   C) Symdeko is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of cystic fibrosis (CF).

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Symdeko has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Cystic Fibrosis (CF), Patients with Unknown Cystic Fibrosis Transmembrane Regulator (CFTR) Gene Mutation.** An FDA-cleared CF mutation test should be used to detect the presence of the CFTR mutation prior to use of Symdeko.

2. **Combination Therapy with Orkambi or Kalydeco.** Symdeko contains ivacaftor, the active agent in Kalydeco and part of Orkambi. Symdeko is not indicated in combination with Kalydeco or Orkambi.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

**REFERENCES**


**Other References Utilized**

**HISTORY**

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes*</th>
<th>TAC Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Policy</td>
<td>Approved for FDA-approved indication</td>
<td>02/14/2018</td>
</tr>
<tr>
<td>Annual Revision</td>
<td>No criteria changes</td>
<td>03/06/2019</td>
</tr>
<tr>
<td>Selected Revision</td>
<td>Cystic Fibrosis: Criteria were modified to approve in patients ≥ 6 years of age, previously ≥ 12 years of age.</td>
<td>06/26/2019</td>
</tr>
</tbody>
</table>

TAC – Therapeutic Assessment Committee;* For a further summary of criteria changes, refer to respective TAC minutes available at: [http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx](http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx); FDA – Food and Drug Administration.