



# Louisiana

## tezacaftor/ivacaftor (Symdeko™)

Policy # 00620

Original Effective Date: 05/16/2018

Current Effective Date: 05/16/2018

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

### When Services May Be Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider tezacaftor/ivacaftor (Symdeko™)‡ for the treatment of cystic fibrosis to be **eligible for coverage**.

### Patient Selection Criteria

Coverage eligibility for tezacaftor/ivacaftor (Symdeko) will be considered when the following criteria are met:

- The patient has a documented diagnosis of cystic fibrosis; AND
- The patient is 12 years of age or older; AND
- The patient meets ONE of the following criteria:
  - The patient is homozygous for the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene as detected by an FDA-cleared test; OR
  - The patient has confirmation of one of the following mutations in the CFTR gene as detected by an FDA cleared test: *E56K, P67L, R74W, D110E, D110H, R117C, E193K, L206W, R347H, R352Q, A455E, D579G, 711+3A → G, S945L, S977F, F1052V, E831X, K1060T, A1067T, R1070W, F1074L, D1152H, D1270N, 2789+5G → A, 3272-26A → G, or 3849 + 10kbC → T*; AND
- The drug will not be used in combination with ivacaftor (Kalydeco®)‡ or lumacaftor/ivacaftor (Orkambi®)‡

### When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers tezacaftor/ivacaftor (Symdeko) when patient selection criteria are not met to be **investigational**.\*

### Background/Overview

Cystic fibrosis is a serious genetic disorder affecting the lungs and other organs that ultimately leads to an early death. It is caused by mutations in a gene that encodes for a protein called CFTR that regulates ion (such as chloride) and water transport in the body. The defect in chloride and water transport results in the formation of thick mucus that builds up in the lungs, digestive tract and other parts of the body leading to severe respiratory and digestive problems, as well as other complications such as infections and diabetes.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

tezacaftor/ivacaftor (Symdeko™)

Policy # 00620

Original Effective Date: 05/16/2018

Current Effective Date: 05/16/2018

Symdeko is a combination of the CFTR potentiator, ivacaftor, and tezacaftor which increases the amount of mature CFTR protein delivered to the cell surface. The combined effect of these two drugs is to increase the quantity and function of CFTR at the cell surface which results in increased chloride transport. Symdeko is indicated for treatment of cystic fibrosis in patients 12 years of age and older who are either homozygous for the *F508del* mutation in the CFTR gene (the most common CFTR genotype and associated with severe disease) or who have at least one of the following mutations: *E56K, P67L, R74W, D110E, D110H, R117C, E193K, L206W, R347H, R352Q, A455E, D579G, 711+3A → G, S945L, S977F, F1052V, E831X, K1060T, A1067T, R1070W, F1074L, D1152H, D1270N, 2789+5G → A, 3272-26A → G, or 3849 + 10kbC → T*. If a patient's mutation status is not known, an FDA-cleared cystic fibrosis mutation test should be used to determine whether a CFTR mutation is present. Symdeko is supplied as co-packaged tezacaftor 100mg/ivacaftor 150 mg fixed-dose combination tablets and ivacaftor 150 mg tablets. Patients should take one combination tablet in the morning and one ivacaftor tablet in the evening. Both doses should be taken with a fat-containing food to ensure adequate absorption. Examples of foods that contain fat are those prepared with butter or oils or those containing eggs, cheeses, nuts, whole milk, or meats.

Because Symdeko contains ivacaftor, the active agent in Kalydeco and part of Orkambi, it should not be used in combination with Kalydeco or Orkambi.

## **FDA or Other Governmental Regulatory Approval** **U.S. Food and Drug Administration (FDA)**

Symdeko was approved by the FDA in February 2018 for the treatment of patients with cystic fibrosis aged 12 years and older who are homozygous for the *F508del* mutation or who have at least one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.

## **Rationale/Source**

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Symdeko was evaluated in two trials in different patient populations. The EVOLVE trial evaluated 510 patients 12 years and older who were homozygous for the *F508del* mutation in the CFTR gene. These subjects were randomized to placebo or Symdeko for 24 weeks. Treatment with Symdeko resulted in modest improvement in FEV1 (absolute change, 4 percentage points versus placebo), and modest improvement in disease-related quality of life score (5.1 points versus placebo). The rate of pulmonary exacerbations was 35% lower in the treatment group compared with placebo (HR 0.64, 95% CI, 0.46-0.88). BMI increased slightly during the 24 week study, but was not significantly different between the study groups.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

tezacaftor/ivacaftor (Symdeko™)

Policy # 00620

Original Effective Date: 05/16/2018

Current Effective Date: 05/16/2018

The EXPAND trial evaluated 248 patients 12 years and older who were heterozygous for the *F508del* mutation and had a residual function mutation and mild or moderate cystic fibrosis-related lung disease. The patients were randomized in a crossover study to Symdeko alone, ivacaftor (Kalydeco) monotherapy, or placebo. Treatment with Symdeko resulted in modest improvement in FEV1 (absolute change, 6.8 percentage points versus placebo), as did ivacaftor monotherapy (absolute change, 4.7 percentage points versus placebo). The benefit of Symdeko compared to Kalydeco was slight, but statistically significant (Absolute change, 2.1 percentage points). Symdeko also resulted in clinically significant improvements in a disease-related quality of life score (11.1 points versus placebo).

## References

1. Symdeko [package insert]. Vertex Pharmaceuticals. Boston, MA. February 2018
2. Symdeko prior authorization document. Express Scripts. Updated February 2018.
3. UpToDate. Cystic fibrosis: Overview of the treatment of lung disease. Accessed April 2018.

## Policy History

Original Effective Date: 05/16/2018

Current Effective Date: 05/16/2018

05/03/2018 Medical Policy Committee review

05/16/2018 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 05/2019

\*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
  1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
  2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.