

Clinical Policy: Tezacaftor/Ivacaftor; Ivacaftor (Symdeko)

Reference Number: CP.PHAR.377

Effective Date: 04.03.18

Last Review Date: 02.19

Line of Business: Commercial, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Tezacaftor/ivacaftor; ivacaftor (Symdeko[™]) is a combination drug for cystic fibrosis (CF).

- Tezacaftor facilitates the cellular processing and trafficking of normal and select mutant forms of cystic fibrosis transmembrane conductance regulator [*CFTR*; (including *F508del-CFTR*)] to increase the amount of mature *CFTR* protein delivered to the cell surface.
- Ivacaftor is a *CFTR* potentiator that facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the *CFTR* protein at the cell surface.
- The combined effect of tezacaftor and ivacaftor is increased quantity and function of *CFTR* at the cell surface, resulting in increases in chloride transport.

FDA Approved Indication(s)

Symdeko is indicated for the treatment of patients with CF 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.

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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Symdeko is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cystic Fibrosis (must meet all):

1. Diagnosis of CF;
2. Age \geq 12 years;
3. One of the following (a or b):
 - a. Member is homozygous for the *F508del* mutation in the *CFTR* gene;
 - b. Presence of at least one mutation in the *CFTR* gene that is responsive to Symdeko based on *in vitro* data and/or clinical evidence (*see Appendix D*);
4. Dose does not exceed tezacaftor 100 mg/ivacaftor 300 mg per day (1 tablet tezacaftor/ivacaftor and 1 tablet ivacaftor per day).

Approval duration:

Medicaid – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Cystic Fibrosis (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed tezacaftor 100 mg/ivacaftor 300 mg per day (1 tablet tezacaftor/ivacaftor and 1 tablet ivacaftor per day).

Approval duration:

Medicaid – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CF: cystic fibrosis

CFTR: cystic fibrosis transmembrane conductance regulator

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Symdeko

CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Symdeko					
2789+5G→A	A455E	D579G	F1074L	R1070W	S945L
3272-26A→G	D110E	E193K	F508del*	R117C	S977F
3849+10kbC→T	D110H	E56K	K1060T	R347H	
711+3A→G	D1152H	E831X	L206W	R352Q	
A1067T	D1270N	F1052V	P67L	R74W	

*A patient must have two copies of the *F508del* mutation or at least one copy of a responsive mutation presented in this table to be indicated.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CF	<p>Adults, adolescents, and children ≥ 12 years: one tablet (tezacaftor 100 mg/ivacaftor 150 mg) PO in the morning and one tablet (ivacaftor 150 mg) in the evening, approximately 12 hours apart with fat-containing food.</p> <p>Reduce dose in patients with moderate and severe hepatic impairment.</p> <p>Reduce dose when co-administered with drugs that are moderate or strong CYP3A inhibitors.</p>	<p>ezacaftor 100 mg/ivacaftor 300 mg per day</p>

VI. Product Availability

Tablets: co-packaged as tezacaftor 100 mg/ivacaftor 150 mg fixed dose combination tablets and ivacaftor 150 mg tablets

VII. References

1. Symdeko Prescribing Information. Boston, MA: Vertex Pharmaceuticals Incorporated; February 2018. Available at: <https://www.symdeko.com/>. Accessed November 9, 2018.
2. Ren CL, Morgan RL, Oermann C, et al. Cystic Fibrosis Foundation pulmonary guidelines: Use of cystic fibrosis transmembrane conductance regulator modulator therapy in patients with cystic fibrosis. *Ann Am Thorac Soc.* 2018; 15(3): 271-280.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.03.18	05.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	10.16.18	02.19

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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