February 19, 2020

Pharmacy and Therapeutics (P&T) Committee
Iowa Medicaid Enterprise

Dear Members of the Iowa Pharmacy and Therapeutics Committee:

On behalf of people in Iowa living with cystic fibrosis (CF), we write to comment on the review of elexacaftor/tezacaftor/ivacaftor (Trikafta™). We urge Iowa Medicaid to include elexacaftor/tezacaftor/ivacaftor (Trikafta™) on the preferred drug list (PDL) for all cystic fibrosis patients age 12 years and older who have at least one copy of the *F508del* mutation in the *CFTR* gene per the Food and Drug Administration's (FDA) label.[1]

About Cystic Fibrosis & the CF Foundation
Cystic fibrosis is caused by genetic mutations that result in the absence or malfunction of a protein known as the cystic fibrosis transmembrane conductance regulator (CFTR). CF causes the body to produce thick, sticky mucus that clogs the lungs and digestive system, which can lead to life-threatening infections. Cystic fibrosis is both serious and progressive; lung damage caused by infection is irreversible and can have a lasting impact on length and quality of life. As the world's leader in the search for a cure for CF the Cystic Fibrosis Foundation accredits more than 130 care centers nationally, including 3 in Iowa. These care centers provide multidisciplinary, patient-centered, specialized care in accordance with systematically reviewed, evidence-based clinical practice guidelines.

About Elexacaftor/Tezacaftor/Ivacaftor
For eligible patients, elexacaftor/tezacaftor/ivacaftor is the most significant therapeutic advance in CF to date. This oral therapy addresses the underlying cause of cystic fibrosis – CFTR protein defects – in individuals with at least one copy of the *F508del* mutation in the *CFTR* gene. Among the modulator class, elexacaftor/tezacaftor/ivacaftor is considered a highly effective therapy. Restoring CFTR function would preserve health and lung function, reduce costly hospitalizations, improve quality of life, and ultimately delay premature death. Longer-term data from first-generation modulators show these improvements are sustained over time, however, modulators cannot reverse existing organ damage.[2] For these reasons, elexacaftor/tezacaftor/ivacaftor should be initiated as soon as patients and their physicians determine it is medically necessary.

For those with one copy of *F508del*, clinical trial data shows significant improvements in lung function (FEV_1), sweat chloride, body mass index (BMI), and the CF Questionnaire-Revised Respiratory Domain (CFQ-R RD, a measure of quality of life) as well as a 63% lower annualized rate of pulmonary exacerbations compared to placebo.[3] Clinical trial subgroup analyses also show a similar improvement in lung function among individuals with baseline lung function under 40% FEV_1 as seen in the overall population.

For individuals homozygous for *F508del*, clinical trial results show sizeable additional improvements in FEV_1, BMI, and CFQ-R RD compared to tezacaftor/ivacaftor indicating those already on a modulator will see considerable additional improvements when changing to this new therapy.[4] Furthermore,

elexacaftor/tezacaftor/ivacaftor has a reduced likelihood of adverse events compared to lumacaftor/ivacaftor. Patients on the triple combination therapy may experience fewer adverse events compared to their current modulator.

CF clinicians are best positioned to determine which treatment will be most effective for each individual given their health status, treatment regimen, and mutation profile.

Policy Recommendations
The CF Foundation urges Iowa Medicaid to make elexacaftor/tezacaftor/ivacaftor available to all eligible CF patients per the FDA label.

We stand ready to answer any questions about elexacaftor/tezacaftor/ivacaftor or other CF treatments. We would be happy to connect you with local CF experts to further discuss this important issue.

Sincerely,

[1] Trikafta™ (elexacaftor/tezacaftor/ivacaftor) [package insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; 2019.

[2] Volkova, N et al. "Disease Progression in patients with cystic fibrosis treated with ivacaftor: Data from national US and UK registries". *Journal of Cystic Fibrosis* (2019)*:* [e-pub]

[3] Middleton, P.G., et al. "Elexacaftor-tezacaftor-ivacaftor for cystic fibrosis with a single Phe508del allele." *NEJM* (2019): [e-pub]

[4] Heijerman, Harry G. M., et al. "Efficacy and safety of the elexacaftor plus tezacaftor plus ivacaftor combination regimen in people with cystic fibrosis homozygous for the F508del mutation: a double-blind, randomized, phase 3 trial." *The Lancet* (2019): [e-pub]