CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS

November 19, 2015

Megan Herink, PharmD
Drug Use Research & Management Program
OHA Division of Medical Assistance Programs
500 Summer Street NE, E35
Salem, OR 97301-1079

Dear Dr. Herink,

On behalf of patients and families with cystic fibrosis (CF), we write to urge you not to place coverage limitations on lumacaftor/ivacaftor (Orkambi™) for patients with lung function values that fall outside the 40-90% range who would otherwise be eligible for this therapy.

Cystic fibrosis is caused by a genetic mutation that results in the malfunction of a protein known as the cystic fibrosis transmembrane conductance regulator (*CFTR*). Decreased CFTR function causes irreversible damage and the associated symptoms of cystic fibrosis and leads to early death, usually by respiratory failure. As the world's leader in the search for a cure for CF and an organization dedicated to ensuring access to high quality, specialized CF care, the Cystic Fibrosis Foundation accredits 120 care centers, including 3 in Oregon, and 55 affiliate programs nationally that provide multidisciplinary, patient-centered care in accordance with systematically reviewed, data-driven, clinical practice guidelines.

Treatment options for this rare, life-threatening disease are extremely limited. For individuals aged 12 years and older with two copies of the *F508del* mutation in the CF gene, Orkambi targets the underlying cause of CF rather than addressing the symptoms and clinical manifestations. This can in turn prevent permanent, irreversible lung damage that currently characterizes the disease and leads to early death.

Clinical trials inclusion parameters such as FEV_1 should not preclude access to this lifesaving therapy for patients that fall within the Food and Drug Administration's (FDA) approved label. Restricting access for patients with lung functions greater than 90% or less than 40% is not grounded in evidence. This drug has been deemed safe and effective for all individuals with CF aged 12 and over homozygous for the *F508del* mutation. There is no basis to conclude that patients who meet FDA label requirements would not benefit from Orkambi.

People with cystic fibrosis experience an average decline in lung function of 1-3% per year (CF Patient Registry, 2013). Even with exemplary treatment compliance on symptomatic therapies, lung infections are common and many patients experience chronic exacerbations requiring hospital visits, additional therapies, and treatment with antibiotics. For all patients with cystic fibrosis, but especially those with diminished FEV_1 values, seemingly modest increases in lung function can yield great benefits in health and quality of life. Thus, patients with FEV_1 values below 40% would experience the most significant clinical benefit. Phase 3 trial results indicated that patients with lung function below 40% actually demonstrated greater improvements in FEV_1 than the over 40% group[1]. Additionally, ongoing studies have thus far not indicated safety

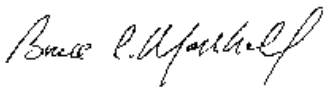
[1] Wainwright, et. al. N Engl J Med, 2015; doi:10.1056/NEJMoa1409547

concerns, which is consistent with the FDA's decision to approve Orkambi without lung function limitations. It is critical for providers to closely monitor improvement and potential adverse effects for this subset of patients, but patients certainly should not be denied this lifesaving drug.

For individuals with FEV_1 values above 90%, Orkambi represents the opportunity to preserve healthy lung function. Initiating treatment with modulators early in disease progression helps to ensure patients have the greatest potential for overall lifetime benefit. Appropriate treatment has the potential to slow the progressive decline in health and prevent irreversible organ damage (lung, pancreas, etc.) characteristic of cystic fibrosis. For individuals near the 90% threshold who may fluctuate above and below this value, restricting access would require individuals to consistently get sicker before getting back on drug. It is not medically reasonable or responsible to withhold an effective treatment until the patient suffers an irreversible decline in health and loss of lung function.

As you review authorization and reauthorization criteria for this life-saving new drug, please consider us a resource. Please do not hesitate to contact Lisa Feng, Senior Director for Coverage & Reimbursement, at lfeng@cff.org or 240-200-3792 with questions or for more information.

Sincerely,



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