May 3, 2019

Vice Admiral Raquel C. Bono
Director
Defense Health Agency
7700 Arlington Blvd.
Suite 5101
Falls Church, VA 22042-5101

Re: Non-medical switching of pancreatic enzyme replacement therapy

Dear Vice Admiral Bono:

Aimed Alliance is a nonprofit organization that works to protect and enhance the rights of health care consumers and providers.

In February 2019, the Department of Defense's (DoD) Pharmacy & Therapeutics (P&T) Committee determined that there is a high degree of interchangeability among pancreatic enzyme replacement therapies (PERTs) and recommended to the Benefit Advisory Panel (BAP) that TRICARE exclude from its coverage all but one PERT product. In March 2019, the BAP elected not to ratify this recommendation and instead instructed the P&T Committee to create a new pathway for patients to access other PERT products.

We are writing to you today to express our gratitude to the DoD's BAP for preserving access to multiple PERT products. If the BAP panel had accepted the P&T Committee's recommendation, individuals with exocrine pancreatic insufficiency (EPI), a condition that impacts highly vulnerable patient populations, including those with cystic fibrosis, would have lost access to medically necessary enzyme treatments.

We also encourage you to remove step therapy protocols for this class of medications to ensure that patients have equitable and unrestricted access to available treatment options.

I. What is EPI?

EPI is a condition that occurs when the human body is unable to provide an adequate supply of digestive enzymes.[1] The shortage of digestive enzymes is commonly caused by other conditions that affect the pancreas, such as cystic fibrosis, Shwachman-Diamond syndrome, pancreatic tumors, and chronic pancreatitis. Patients with this condition are unable to properly digest food, which causes gastrointestinal upset and difficulty absorbing nutrients from food. Patients with EPI rely on PERTs, which replace missing enzymes and help break down nutrients in food. If the body does not absorb enough nutrients, it can cause further complications. For example, Vitamin K insufficiencies can cause bleeding disorders and Vitamin D insufficiencies

[1] https://www.identifyepi.com/what-is-epi

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can cause bone pain.[2] For individuals with cystic fibrosis in particular, lack of proper treatment can be life-threatening.[3] Therefore, patients with EPI rely on these medications for survival.[4]

II. PERT Interchangeability and Nonmedical Switching

While there are six FDA-approved PERT products available in the United States, the FDA has determined that none of these medications are interchangeable, meaning that they do not "produce the same clinical results as the reference product in any given patient."[5] As such, the P&T Committee's original recommendation to exclude all but one PERT from TRICARE's Uniform Formulary could have resulted in the non-medical switching of a vulnerable patient population. Non-medical switching occurs when an insurer requires a stable patient to switch from his or her current, effective medication to an alternative drug by excluding the original medication from coverage, elevating the drug to a higher cost tier, or otherwise limiting access to a treatment or increasing the patient's out-of-pocket costs. The patient is forced to switch to a "therapeutically equivalent" medication based on the actions of the payer rather than for medical reasons. Therapeutically equivalent drugs do not need to be chemically equivalent, bioequivalent, or generically equivalent.[6] They can be entirely different medications.

A switch to a different PERT product could result in harm to patients. Each PERT product has a different formulation and different dosing.[7] As such, forcing a patient to switch from one PERT to another could upset the patient's stability and expose him or her to unnecessarily negative health outcomes, including abdominal pain, intestinal obstruction, increased incidence of steatorrhea, and rectal prolapse.[8] If a patient with EPI is switched to a PERT that does not adequately manage his or her condition, the symptoms of the condition could become exacerbated and could progress into more serious health conditions. For example, a patient could develop osteoporosis as a result of inadequate Vitamin D levels, or a patient could experience ataxia and peripheral neuropathy as a result of inadequate Vitamin E levels.[9] Furthermore, switching between these products carries the risk that the body will develop tolerance to the active ingredients and, consequently, the medication's efficacy could be diminished.[10]

PERTs allow individuals with conditions such as cystic fibrosis to maintain or gain weight, which is vital, especially in pediatric populations.[11] Children with cystic fibrosis who are unable to reach the 50th weight-for-age percentile are at a greater risk of acute pulmonary exacerbations, impaired glucose tolerance, and cystic fibrosis-related diabetes; spend more days

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[2] https://www.webmd.com/digestive-disorders/exocrine-pancreatic-insufficiency#1
[3] https://www.medicalnewstoday.com/articles/147960.php
[4] https://www.pharmacytimes.com/publications/issue/2008/2008-12/p2ppeps-1208
[5] https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580419.htm
[6] http://www.gabionline.net/Biosimilars/General/Glossary-of-key-terms.
[7] https://www.verywellhealth.com/pancrelipase-pancreatic-enzyme-replacement-998342
[8] https://www.pharmacytimes.com/publications/issue/2008/2008-12/p2ppeps-1208;
[9] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5873407/
[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5706924/
[11] https://www.ncbi.nlm.nih.gov/pubmed/23062247

in the hospital; and have incrementally lower survival at age 18.[12] Given that PERT products are not interchangeable, patients may experience detrimental weight loss when they are switched and as they struggle to find the appropriate dose on the new product. As such, patients must be allowed to stay on their current therapy.

III. Step Therapy

While the BAP has determined that it will not exclude a PERT medication from coverage, that same medication will still be subject to a step therapy protocol. Step therapy policies, also referred to as "fail first," require individuals to try and fail on less expensive treatments, sometimes with adverse effects, before the insurer will cover the prescribed treatment. Step therapy policies can be unethical and inconsistent with standards of care, resulting in interference with the practitioner-patient relationship and significant delays in access to prescribed treatments. We request that you reconsider implementing step therapy in this class of medications to ensure that patients have equitable and unrestricted access to the available treatment options.

IV. Conclusion

As the BAP has recognized, the decision to switch treatments should remain within the discretion of the treating health care provider and patient, and it should be made on a case-by-case basis with the support of scientific evidence and the patient's full consent.[13] Patients with chronic conditions like EPI must often try various doses of PERT before they find the dose that works for them, and doses vary from product to product.[14] Once stable on a therapy, it is critically important that these patients are able to remain on the same therapy to ensure that they can successfully manage their health.

We would like to reiterate our gratitude to the BAP for preserving access to multiple PERT options for patients with EPI and request that you reconsider implementing step therapy protocols regarding these medications. If you would like to discuss this matter further, you can reach us at (202) 559-0380 or jwylam@aimedalliance.org.

Sincerely,

John Wylam

Staff Attorney

[12] https://www.ncbi.nlm.nih.gov/pubmed/23062247
[13] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5486595/