Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Pancreatic Enzymes for Chronic Pancreatitis***
-May 2018-

Background:

The National Pharmacy & Therapeutics Committee (NPTC) discussed the role of pancreatic enzyme replacement therapy (PERT) in chronic pancreatitis at the May 2018 meeting. Currently, there are no pancreatic enzyme products on the Indian Health Service National Core Formulary. Following delivery of both clinical and pharmacoeconomic reviews of PERT including agency procurement and utilization trends, the **NPTC made no modifications to the National Core Formulary**.

Discussion:

Chronic pancreatitis is an inflammatory disease of the pancreas characterized by progressive fibrosis, calcifications, and dilated pancreatic duct. These conditions lead to irreversible structural changes resulting in impairment of both exocrine and endocrine functions[1]. Exocrine pancreatic insufficiency (EPI) results in a decreased synthesis or secretion of pancreatic enzymes and bicarbonate leading to maldigestion of food and subsequently malabsorption of nutrients[2]. Pancreatic enzymes are used in EPI to supplement these deficiencies. Pancrelipase is a mixture of the digestive enzymes amylase, lipase, and protease which acts locally in the duodenum to break down nutrients to assist absorption.

In the United States the incidence, prevalence, and mortality reported for chronic pancreatitis vary due to differences in study design, diagnostic criteria, and geography. Prevalence of chronic pancreatitis ranges from 0.04% to 5% and incidence ranges from 1.6 to 23 cases per year per 100,000 people[3-4]. In 1999, chronic pancreatitis was responsible for 3289 deaths in the US, ranking as the 235th leading cause of death[5]. There is limited data to establish rates of chronic pancreatitis among American Indians and Alaska Natives. Relying on limited national epidemiology data, rates of chronic pancreatitis remain low.

Efficacy data for pancreatic enzymes is limited. Prior to 2010, there were no FDA regulations on pancreatic enzymes. In 2006, the FDA issued a statement that outlined the requirements that manufacturers would have to meet to ensure that a PERT product was effective, safe, and of sufficient quality for FDA approval[6].

A 2009 Cochrane review attempted to pool all data from currently available randomized control trials. While all studies (N=10) showed a significant reduction in fecal fat (-1.03 grams/day; 95% CI -1.60 to -0.46), due to small sample sizes and variations in study design, results from these studies could not be pooled for reporting of clinically important outcomes (e.g., pain reduction, incidence of steatorrhea and analgesic consumption)[7]. In 2017, a meta-analysis of 7 randomized control trials was published involving 282 participants with chronic pancreatitis or post-pancreatic surgery. Authors similarly concluded that PERT was effective and tolerable in EPI patients however they also noted the need for larger and higher quality studies on EPI to determine the long-term effects of standard PERT treatment[8]. A subsequent 2017 meta-analysis published by BMJ reviewed 17 randomized control trials involving 511 participants with chronic pancreatitis. Results indicated that PERT increased the coefficient of fat absorption versus baseline (2.28, 1.50 to 3.06; $p<0.00001$) but with high heterogeneity ($I^2=89\%$) across the studies. Data also showed that PERT increased the coefficient of fat absorption over placebo (1.67, 0.81 to 2.53; $p=0.0001$) but again noted high study heterogeneity ($I^2=86\%$). They found no statistical results for high dose vs. low dose pancreatic enzymes or for enteric-coated microspheres vs. non-coated microspheres[9]. Due to the paucity of available literature on PERT, all aforementioned meta-analyses concluded that larger and more robust studies were needed to further assess safety and efficacy[7-9].

Guidelines from both the Italian Consensus Guidelines for Chronic Pancreatitis and the Australasian Guidelines for the Management of Pancreatic Exocrine Insufficiency recommend the use of PERT in chronic pancreatitis patients with EPI. They differ in their dosing strategies but agree that dosing should be patient specific. The American College of Gastroenterology (see Chronic Pancreatitis section) is due to release guidelines on chronic pancreatitis in mid to late 2018[10-11].

Findings:

There is limited evidence to support that PERT improves fat absorption in comparison to baseline and placebo. Presently, no major differences exist amongst products and all agents are superior to placebo for improving fat malabsorption associated with EPI. There is no statistically significant evidence to substantiate the use of PERT for pain reduction. Long term safety and efficacy data is needed to establish and support extended PERT duration. Product selection should be based around acquisition cost and range of available dosage strengths to accommodate for individualized dosing.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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