MEDCO FORUM®
PRESENTING INNOVATIVE PRODUCTS AND SERVICES TO HEALTHCARE PROFESSIONALS
VOLUME 19 NUMBER 48
OCTOBER 2012
REPRINT

VIOKACE™ (PANCRELIPASE) IS THE ONLY FDA-APPROVED PANCREATIC ENZYME PRODUCT WITHOUT AN ENTERIC COATING

VIOKACE™, in combination with a proton pump inhibitor (PPI), is indicated in adults for the treatment of exocrine pancreatic insufficiency (EPI) due to chronic pancreatitis or pancreatectomy.[1]

VIOKASE® was previously marketed for 18 years in the United States under the company name Axcan Pharma US, Inc. now known as Aptalis Pharma US, Inc. Aptalis Pharma US, Inc. is a global specialty pharmaceutical company focused on gastrointestinal diseases and cystic fibrosis.

In 2004, the FDA required all manufacturers of pancreatic enzyme products to submit NDAs in order to remain on the market. Aptalis Pharma™ performed all requisite clinical studies and submitted a new drug application for VIOKACE and in March 2012, the U.S. Food and Drug Administration (FDA) approved VIOKACE™ (pancrelipase) tablets.

VIOKACE, in combination with a PPI, is used to treat adults with EPI, due to chronic pancreatitis or those who have undergone pancreatectomy who cannot digest food normally because they lack needed enzymes or because their enzymes are not released into the intestine.[1] VIOKACE is a combination of porcine-derived lipases, proteases, and amylases and is available in two dosage strengths[1]:

- VIOKACE™ (pancrelipase) Tablets containing 20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase

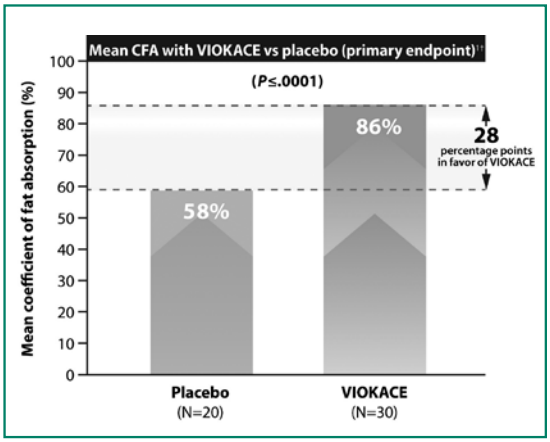

Figure 1

- VIOKACE™ (pancrelipase) Tablets containing 10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase

Principal Investigator Dr. Phillip Toskes

Dr. Phillip Toskes, Professor of Medicine in the Division of Gastroenterology, Hepatology, and Nutrition at the University of Florida College of Medicine in Gainesville, FL reports: "VIOKACE is an enzyme that I have evaluated extensively. Because VIOKACE is uncoated, there is no capsule or enteric coating to dissolve as it passes through the duodenum, which means that the proteases are delivered directly into the proximal small bowel.[2] It is important to deliver sufficient enzymes to the proximal duodenum where nutrients are digested to correct maldigestion and decrease steatorrhea."

As an international authority on pancreatic and malabsorptive disorders, Dr. Toskes participated in a multicenter, randomized, parallel-group, placebo-controlled, double-blind study of 50 patients, ages 24 to 70 years, with EPI due to chronic pancreatitis or pancreatectomy. Eighteen patients had a history of pancreatectomy (11 were treated with VIOKACE). After a wash-out period (six or seven days), patients were randomized to a fixed dose of VIOKACE, 22 tablets per day (six tablets with three meals and two tablets with two or three snacks) or placebo, in combination with a proton pump inhibitor.[1] The PPI prevents degradation of lipase as it passes through the acidic gastric juices.

"It is necessary to give PPI therapy along with VIOKACE," Dr. Toskes states.

The duration of exposure ranged from six to seven days. All patients were maintained on a controlled high-fat diet of 100 grams of fat per day. Forty-nine patients completed the double-blind period. The coefficient of fat absorption (CFA) was determined by a 72-hour stool collection during both treatments, when both fat excretion and fat ingestion were measured. At the end of double-blind treatment, the mean CFA was 86% with VIOKACE treatment compared to 58% with placebo.[1] (FIGURE 1) The mean difference in CFA at the end of the double-blind treatment period was 28 percentage points in favor of VIOKACE treatment with 95% Confidence Interval (21,37) and $P \leq .0001$.[1]

Changes in frequency and quality of stools were secondary endpoints of the study. Dr. Toskes noted, "What was observed was a significant reduction in stool frequency vs. placebo." The reduction in stool frequency vs. placebo was a difference of 1.1 less stools per day in those treated with VIOKACE vs. a difference of 0.1 less stools per day in those treated with placebo (p.0083). There was a higher mean proportion of formed/normal stools and lower mean proportion of soft stools, although these findings were not statistically significant.[3]

Enzyme dosing should begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day. Therapy should be initiated at the lowest recommended dose and gradually increased. Individualize dosage based on clinical symptoms, the degree of steatorrhea present, and the fat content of the diet.[1]

Important Safety Information

Fibrosing colonopathy is associated with high-dose use of pancreatic enzyme replacement. Exercise caution when doses of VIOKACE exceed 2,500 lipase units/kg of body weight per meal (or greater than 10,000 lipase units/kg of body weight per day).To avoid irritation of oral mucosa, do not chew VIOKACE or retain in the mouth. Exercise caution when prescribing VIOKACE to patients with gout, renal impairment, or hyperuricemia. There is theoretical risk of viral transmission with all pancreatic enzyme products including VIOKACE. In rare cases, patients taking pancreatic enzyme products with different formulations of the same active ingredient (pancrelipase) have experienced severe allergic reactions including anaphylaxis, asthma, hives, and pruritus. Exercise caution when administering pancrelipase to a patient with a known allergy to proteins of porcine origin. VIOKACE tablets contain lactose monohydrate. Patients who have lactose intolerance may not be able to tolerate VIOKACE. Adverse reactions occurring in at least two chronic pancreatitis or pancreatectomy patients (greater than or equal to 7%) receiving VIOKACE are biliary tract stones and anal pruritus. The safety and effectiveness of VIOKACE in pediatric patients have not been established. VIOKACE use in pediatric patients may result in suboptimal growth due to tablet degradation in the gastric environment. In general, delayed release (enteric-coated) capsules should be used for pediatric patients. VIOKACE is not interchangeable with any other pancrelipase product.

For more information about VIOKACE, please call 1-800-950-8085, or visit our website at www.aptalispharma.com or www.viokace.com.

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References:

1. VIOKACE™ US Prescribing Information; March 2012
2. Forsmark, C. E. (Ed.). (2005). Pancreatitis and Its Complications. (pp. 209 - 221). Totowa, New Jersey: Humana Press Inc.
3. Data on file (VI016EP107-01), Aptalis Pharma US, Inc., Birmingham, AL.