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PRESCRIBING ALERT®

Dear Healthcare Professional,

At *MPR*, we strive to bring you important drug information in a concise and timely fashion. In keeping with this goal, we are pleased to bring you this PRESCRIBING ALERT announcing the FDA approval of Zenpep™ (pancrelipase) Delayed-Release Capsules, from Eurand Pharmaceuticals, Inc., for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.[1]

In accordance with the FDA guidelines for pancreatic enzyme products, ZENPEP was studied in adults and children.[1-3] ZENPEP improved coefficient of fat absorption, a key indicator of nutrient absorption, and reduced gastrointestinal symptoms.[1,4,5]

ZENPEP is designed to deliver 100% labeled lipase, with zero overfill, providing consistent amounts of lipase dose after dose.[4]

Indication

Zenpep™ (pancrelipase) Delayed-Release Capsules is indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.

Adverse reactions

The most common adverse events (≥6% of patients treated with ZENPEP) are abdominal pain, flatulence, headache, cough, decreased weight, early satiety, and contusion. The most serious adverse reactions reported with different pancreatic enzyme preparations of the same active ingredient (pancrelipase) include fibrosing colonopathy, hyperuricemia and allergic reactions.

SELECTED IMPORTANT SAFETY INFORMATION

Fibrosing colonopathy is a rare serious adverse reaction associated with high-dose use of pancreatic enzyme replacement products and most commonly reported in pediatric patients with CF. Exercise caution when doses of ZENPEP exceed 2,500 lipase units/kg of body weight per meal (or greater than 10,000 lipase units/kg of body weight per day).

(Selected Important Safety Information continued on back)

To avoid irritation of oral mucosa or inactivation of enzymes, do not chew ZENPEP capsules or beads or retain in the mouth.

Exercise caution when prescribing ZENPEP to patients with gout, renal impairment, or hyperuricemia.

There is theoretical risk of viral transmission with all pancreatic enzyme products, including ZENPEP.

Exercise caution when administering pancrelipase to a patient with a known allergy to proteins of porcine origin.

More information about ZENPEP is available in the current edition of *MPR*.

For your reference, please see the enclosed full Prescribing Information and Medication Guide for ZENPEP.

Sincerely,

Grace L. McBride
Editorial Director
MPR Custom Programs

REFERENCES: 1. Zenpep [package insert]. Yardley, PA. Eurand Pharmaceuticals, Inc.; 2009. **2.** Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research. Exocrine pancreatic insufficiency drug products; extension to obtain marketing approval [Docket No. 2003N-0205]. *Fed Regist*. 2007;72(207):60860-60862. http://www.access.gpo.gov/su_docs/fedreg/a071026c.html. Published October 26, 2007. Accessed September 18, 2009. **3.** Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research. Guidance for industry: exocrine pancreatic insufficiency drug products—submitting NDAs. 2006. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071651.pdf. Published April 2006. Accessed September 18, 2008. **4.** Data on file. Eurand SpA. Milan, Italy. **5.** Wooldridge JL, Heubi JE, Amaro-Galvez R, et al. EUR-1008 pancreatic enzyme replacement is safe and effective in patients with cystic fibrosis and pancreatic insufficiency. *J Cyst Fibros*. 2009; doi:10.1016/j.jcf.2009.07.006.

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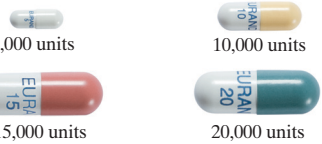
Zenpep™

(pancrelipase) Delayed-Release Capsules

Company: Eurand Pharmaceuticals, Inc. ℞
Active ingredients: Pancrelipase (porcine-derived lipases, amylases, and proteases); lipase 5,000 units (amylase 27,000 units; protease 17,000 units); lipase 10,000 units (amylase 55,000 units; protease 34,000 units); lipase 15,000 units (amylase 82,000 units; protease 51,000 units); lipase 20,000 units (amylase 109,000 units; protease 68,000 units). Delayed-Release Capsules.
Indication: Treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.
Adults: Take during meal/snack. Swallow whole; do not crush or chew. Initiate 500 lipase units/kg per meal; max 2,500 lipase units/kg per meal (≤10,000 lipase units/kg daily) or <4,000 lipase units/g fat daily. Dosing limitations and Administration: see Prescribing Information.
Children: ≤12mo: 2,000-4,000 lipase units/120 mL formula or per breastfeeding; avoid mixing with formula or breast milk. >12mo to <4yrs: 1,000 lipase units/kg to 2,500 lipase units/kg per meal (≤10,000 lipase units/kg daily) or <4,000 lipase units/g of fat daily. >4yrs: initiate 500 lipase units/kg per meal; max 2,500 lipase units/kg per meal (≤10,000 lipase units/kg daily) or <4,000 lipase units/g fat daily. Dosing limitations and Administration: see Prescribing Information.
Warnings & Precautions: Risk of fibrosing colonopathy. Irritation of oral mucosa. Risk of hyperuricemia. There is a theoretical risk of viral transmission. Allergic reactions. Pregnancy (Cat. C) Nursing mothers. (See back for full detail).
Adverse reactions: Abdominal pain, flatulence, headache, cough, decreased weight, early satiety, contusion.
How supplied: Caps—5,000 units: 100; 10,000 units: 100; 15,000 units: 100; 20,000 units: 100, 500



5,000 units | 10,000 units | 15,000 units | 20,000 units

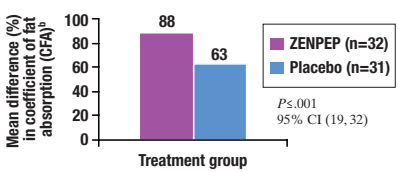
Approved for use in children and adults

☑ ZENPEP is FDA-approved for the treatment of exocrine pancreatic insufficiency (EPI) due to cystic fibrosis (CF) or other conditions[1]

- Approval based on 2 studies in children and adults with CF[1]

STUDY 1: EFFICACY OF ZENPEP VS PLACEBO

Primary Efficacy End Point in Study 1[a] (N=34)



[a]Study 1 was a randomized, double-blind, placebo-controlled, crossover, multicenter study in patients (N=34) with EPI associated with CF aged ≥7 years.. Patients were randomized to receive ZENPEP or matching placebo for 6 to 7 days of treatment, followed by crossover to the alternate treatment for an additional 6 to 7 days. The mean dose during the controlled treatment periods ranged from a mean dose of 3,900 lipase units/kg/day to 5,700 lipase units/kg/day. All patients consumed a high-fat diet (≥100 g of fat/day) during the treatment period.

[b]CFA was determined by a 72-hour stool collection during both crossover treatment periods, when both fat excretion and fat ingestion were measured. CFA during placebo treatment was used as the no-treatment CFA value.

Source: ZENPEP [package insert].[1]

☑ ZENPEP is a pancreatic enzyme product that meets the FDA guidelines to ensure delivery of 100% of labeled lipase dose[1-3]

- Provides consistent amount of lipase in every dose[1]
- Significantly improves CFA, a key indicator of nutrient absorption, and reduces gastrointestinal symptoms[1,4,5]
- Offers a proven safety profile as demonstrated in clinical trials in adults, adolescents, and children as young as 1 year[1,4]

(continued on back)

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- ZENPEP is easy to switch to, easy to start, and easy to take, with 4 strengths for dosing precision[5]
  - — ZENPEP is not interchangeable with any other pancrelipase product and requires a new prescription and titration for symptom control

ZENPEP dosing and administration

- Capsules should be taken whole with meals or snacks and with sufficient amount of fluid[1]
- Capsules may also be opened. Contents should be sprinkled onto small amounts of acidic (pH ≤4.5) soft foods (eg, commercially available applesauce, bananas, pears) and taken immediately, followed by water or juice[1]
- To avoid irritation of oral mucosa or enzyme inactivation, ZENPEP capsules or beads should not be chewed or retained in the mouth[1]

In clinical studies, the incidence and type of adverse events reported were similar in children (7-11 years), adolescents (12-16 years), and adults (>18 years)

- The most common adverse events (≥6% of patients treated with ZENPEP) are abdominal pain, flatulence, headache, cough, decreased weight, early satiety, and contusion.
- The most serious adverse reactions reported with different pancreatic enzyme preparations of the same active ingredient (pancrelipase) include fibrosing colonopathy, hyperuricemia and allergic reactions.

Indication

Zenpep™ (pancrelipase) Delayed-Release Capsules is indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.

SELECTED IMPORTANT SAFETY INFORMATION

- Fibrosing colonopathy is a rare serious adverse reaction associated with high-dose use of pancreatic enzyme replacement products and most commonly reported in pediatric patients with CF. Exercise caution when doses of ZENPEP 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 or inactivation of enzymes, do not chew ZENPEP capsules or beads or retain in the mouth.
- Exercise caution when prescribing ZENPEP to patients with gout, renal impairment, or hyperuricemia.
- There is theoretical risk of viral transmission with all pancreatic enzyme products including ZENPEP.
- Exercise caution when administering pancrelipase to a patient with a known allergy to proteins of porcine origin.

Adverse reactions

The most common adverse events (≥6% of patients treated with ZENPEP) are abdominal pain, flatulence, headache, cough, decreased weight, early satiety, and contusion. The most serious adverse reactions reported with different pancreatic enzyme preparations of the same active ingredient (pancrelipase) include fibrosing colonopathy, hyperuricemia and allergic reactions.

Please see accompanying full Prescribing Information and medication guide and provide to medication guide patients prescribed ZENPEP.

REFERENCES: 1. Zenpep [package insert]. Yardley, PA. Eurand Pharmaceuticals, Inc.; 2009. **2.** Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research. Exocrine pancreatic insufficiency drug products; extension to obtain marketing approval [Docket No. 2003N-0205]. *Fed Regist.* 2007;72(207):60860-60862. http://www.access.gpo.gov/su_docs/fedreg/a071026c.html. Published October 26, 2007. Accessed September 18, 2009. **3.** Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research. Guidance for industry: exocrine pancreatic insufficiency drug products—submitting NDAs. 2006. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071651.pdf. Published April 2006. Accessed September 18, 2008. **4.** Data on file. Eurand SpA. Milan, Italy. **5.** Wooldridge JL, Heubi JE, Amaro-Galvez R, et al. EUR-1008 pancreatic enzyme replacement is safe and effective in patients with cystic fibrosis and pancreatic insufficiency. *J Cyst Fibros.* 2009; doi:10.1016/j.jcf.2009.07.006.

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