

## EPANOVA Fact Sheet

### ABOUT EPANOVA

- EPANOVA<sup>®</sup> (omega-3-carboxylic acids) is a free fatty acid form of omega-3 that is approved by the US Food and Drug Administration (FDA) as an adjunct to diet to reduce triglyceride (TG) levels in adults with severe hypertriglyceridemia (triglyceride levels greater than or equal to 500 mg/dL)<sup>1</sup>
  - EPANOVA is the first FDA approved prescription omega-3 in free fatty acid form<sup>2</sup>
- EPANOVA contains multiple omega-3 fatty acids (EPA (Eicosapentaenoic Acid) and DHA (Docosahexaenoic Acid) being the most abundant)<sup>1</sup>
- The dosage of EPANOVA is 2 grams (2 capsules) or 4 grams (4 capsules), making it the first prescription omega-3 to have a dosing option as few as two capsules once a day.<sup>1</sup> It can be taken with or without food<sup>1</sup>
- EPANOVA strengthens the company's existing portfolio of medicines

### ABOUT SEVERE HYPERTRIGLYCERIDEMIA

- Triglycerides (TGs) are a type of lipid (fat) found in the blood and an essential energy source for the body.<sup>3</sup> Some people have severely high triglyceride levels, meaning they have too much fat in their blood and that can lead to serious health complications<sup>4,5</sup>
- Nearly four million American adults have severe hypertriglyceridemia and this figure continues to increase along with the incidence of associated conditions, such as obesity and diabetes<sup>4,6</sup>
- The first-line recommendation for reducing TG levels is making lifestyle changes, such as eating a healthy diet, increasing physical activity and losing weight.<sup>7</sup> For some patients, though, lifestyle changes may not be enough to lower very high TG levels and medication may be needed<sup>3</sup>
  - Clinical practice guidelines reinforce the need to lower TG levels in patients with severe hypertriglyceridemia<sup>4,8,9,10</sup>
  - Statins, fibrates, niacin, and omega-3 fatty acids are treatments used to lower very high TGs<sup>5</sup>

### EXISTING EPANOVA DATA

- EVOLVE (EpanoVa fOr Lowering Very high triglyceridEs) was a 12 week, multi-center, randomized, double-blind, placebo (olive oil) controlled study of 399 patients with fasting TG levels  $\geq 500$  mg/dL and  $< 2000$  mg/dL that evaluated the efficacy and safety of EPANOVA versus placebo (olive oil)<sup>1,2</sup>
- Results showed that compared to baseline, EPANOVA 2 grams reduced triglycerides by 25%; EPANOVA 4 grams reduced triglycerides by 31%; versus a reduction of 10% with placebo (olive oil). The difference was statistically significant for each dose of Epanova versus placebo. Treatment with EPANOVA also resulted in statistically significant reductions in non-HDL-C levels compared with placebo, but increased LDL-C levels<sup>1</sup>

### CLINICAL & REGULATORY PLANS

- AstraZeneca is committed to assessing the impact of lowering triglycerides and further evaluating the clinical profile of EPANOVA
- Through a large-scale trial, STRENGTH (a long-term outcomes study to assess STatin Residual risk reduction with EpaNova in hiGh cardiovascular risk paTients with Hypertriglycerideamia), AstraZeneca will evaluate the safety and efficacy of EPANOVA on cardiovascular outcomes in combination with statin therapy in patients with mixed dyslipidemia at increased risk of cardiovascular disease
- AstraZeneca also plans to pursue the development of a fixed dose combination of EPANOVA with a statin and plans to file for regulatory approval in other markets for the severe hypertriglyceridemia indication<sup>7</sup>

### About EPANOVA

EPANOVA is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia.

**Usage Considerations:** Patients should be placed on an appropriate lipid-lowering diet before receiving EPANOVA and should continue this diet during treatment with EPANOVA.

Laboratory studies should be done to ascertain that the triglyceride levels are consistently abnormal before instituting EPANOVA therapy. Attempts should be made to control serum lipids with appropriate diet, exercise, weight loss in obese patients, and control of any medical problems such as diabetes mellitus and hypothyroidism that are contributing to the lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed if possible prior to consideration of triglyceride-lowering drug therapy.

#### **Limitations of Use:**

The effect of EPANOVA on the risk of pancreatitis has not been determined.

The effect of EPANOVA on cardiovascular mortality and morbidity in patients has not been determined.

#### **Important Safety Information about EPANOVA**

- EPANOVA is contraindicated in patients with known hypersensitivity to EPANOVA or any of its components
- In some patients, EPANOVA increases LDL-C levels. LDL-C levels should be monitored periodically during therapy with EPANOVA.
- In patients with hepatic impairment, ALT and AST levels should be monitored periodically during therapy with EPANOVA
- EPANOVA should be used with caution in patients with known hypersensitivity to fish and/or shellfish
- Some published studies with omega-3-fatty acids demonstrated prolongation of bleeding time, which did not exceed normal limits and did not produce clinically significant bleeding episodes. Patients taking anti-platelet agents or anticoagulants were excluded from EPANOVA clinical trials involving patients with hypertriglyceridemia. Nonetheless, patients receiving treatment with EPANOVA and an anticoagulant or other drugs affecting coagulation (eg, anti-platelet agents) should be monitored periodically
- Most common adverse reactions with EPANOVA 2 grams and 4 grams, respectively, were diarrhea (7%, 15%), nausea (4%, 6%), abdominal pain or discomfort (3%, 5%) and eructation (3%, 3%)

#### **About AstraZeneca**

AstraZeneca is a global, innovation-driven biopharmaceutical business with a primary focus on the discovery, development and commercialization of prescription medicines for gastrointestinal, cardiovascular, neuroscience, respiratory and inflammation, oncology and infectious disease. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

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EPANOVA is a registered trademark, and AZ&Me is a trademark of the AstraZeneca group of companies.

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<sup>1</sup> Prescribing Information for EPANOVA. AstraZeneca Pharmaceuticals LP, Wilmington, DE.

<sup>2</sup> US Food and Drug Administration. Drugs@FDA. <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>. Accessed May 6, 2014.

<sup>3</sup> Mayo Clinic. Triglycerides: Why do they matter? Available at <http://www.mayoclinic.org/diseases-conditions/high-blood-cholesterol/in-depth/triglycerides/art-20048186?pg=1>. Accessed February 18, 2014.

<sup>4</sup> Miller M, Stone N, et al. Triglycerides and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2011;123:2292-2333. DOI: 10.1161/CIR.0b013e3182160726. Available at <http://circ.ahajournals.org/content/123/20/2292.full.pdf>. Accessed February 18, 2014

<sup>5</sup> Oh, Robert C., et al. Management of Hypertriglyceridemia. *Am Fam Physician*. 2007 May 1;75(9):1365-1371.

<sup>6</sup> Maki K, et al. Treatment options for the management of hypertriglyceridemia. Strategies based on best-available evidence. *Journal of Clinical Lipidology*. 2012; 6: 413-426. DOI: 10.1016/j.jacl.2012.04.003

<sup>7</sup> American Heart Association. Triglycerides. [http://www.heart.org/HEARTORG/GettingHealthy/NutritionCenter/Triglycerides\\_UCM\\_306029\\_Article.jsp](http://www.heart.org/HEARTORG/GettingHealthy/NutritionCenter/Triglycerides_UCM_306029_Article.jsp). Accessed December 16, 2013.

<sup>8</sup> Evaluation of Hypertriglyceridemia: An Endocrine Society Clinical Practice Guideline. 2012. *Journal of Clinical Endocrinology and Metabolism*. 97(9):2969-2989. DOI: 10.1210/jc.2011-3213

<sup>9</sup> American Association of Clinical Endocrinologists Guidelines for Management of Dyslipidemia and Prevention of Atherosclerosis. Available at <https://www.aace.com/files/lipid-guidelines.pdf>. Accessed February 25, 2014.

<sup>10</sup> Standards of Medical Care in Diabetes – 2014. 2014. *Diabetes Care*. 37(1):S14-S80. DOI: 10.2337/dc14-S014.

<sup>11</sup> ClinicalTrials.gov. Outcomes Study to Assess STatin Residual Risk Reduction with EpaNova in High CV Risk PatienTs with Hypertriglyceridemia (STRENGTH) <http://clinicaltrials.gov/ct2/show/NCT02104817?term=strength+epanova&rank=1> Accessed April 29, 2014