Therapeutic Class Overview
Omega-3 Fatty Acids

INTRODUCTION

- The independent relationship of triglycerides (TGs) to the risk of future cardiovascular disease (CVD) events has long been controversial (Miller et al., 2011).
- Rich sources of omega-3-fatty acids come from fatty fish and plant sources, and fish oil has eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).
  - When administered at high doses, they can reduce levels of TGs by approximately 50% (National Cholesterol Education Program [NCEP], 2002; Rosensen, 2013; Tangney, 2013).
  - Select clinical trials suggest that relatively high doses of omega-3-fatty acids, in the form of fish, fish oils or high-linolenic acid oils, will reduce the risk for major coronary events in persons with established coronary heart disease; however, the overall body of literature does not offer convincing evidence that fish oil supplements are beneficial for preventing cardiovascular disease or improving outcomes (NCEP, 2002; Institute for Clinical Systems Improvement, 2017; Smith et al., 2011).
- The scope of this review will focus on LOVAZA®, OMTRYG™ and TRIKLO (omega-3-acid ethyl esters), VASCEPA® (icosapent ethyl), and EPANOVA® (omega-3-carboxylic acids) for their respective Food and Drug administration (FDA)-approved indications, which are outlined in Table 1.
- LOVAZA, OMTRYG and TRIKLO (omega-3-acid ethyl esters), VASCEPA (icosapent ethyl), and EPANOVA (omega-3 carboxylic acids) are FDA-approved prescription omega-3 fatty acids. These products are approved as adjunct therapy to diet to reduce TGs in adults with severe (≥500 mg/dL) hypertriglyceridemia.
  - LOVAZA (omega-3-acid ethyl esters) is available as a 1 gram soft-gelatin capsule, containing approximately 375 mg and 465 mg of DHA and EPA, respectively. TRIKLO is a branded generic product for LOVAZA.
  - VASCEPA (icosapent ethyl) is available as a soft-gelatin capsule, containing ≥95% icosapent ethyl, an esterified formation of EPA (Rosensen, 2013).
  - EPANOVA (omega-3 carboxylic acids) is available as a coated, soft-gelatin capsule, containing at least 850 mg of polyunsaturated fatty acids, including multiple omega-3 fatty acids (predominantly EPA and DHA).
  - OMTRYG (omega-3-acid ethyl esters) is available as a 1.2 gram, transparent, soft-gelatin capsule filled with yellow oil containing 375 mg and 465 mg of DHA and EPA, respectively.
  - Of note, there are several over-the-counter products containing omega-3 fatty acids that are marketed as nutritional supplements. These products do not have FDA-approved indications and may not contain the same amount of the active ingredient (Facts and Comparisons, 2017).
- Omega-3 fatty acids have the potential to be used off-label for the treatment of coronary arteriosclerosis, familial combined hyperlipidemia, heart failure and hyperlipidemia with TG levels < 500 mg/dL (Micromedex, 2017).
- The 2013 American College of Cardiology/American Heart Association (ACC/AHA) Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Disease in Adults focuses more heavily on a patient’s overall atherosclerotic cardiovascular disease (ASCVD) risk versus achieving target LDL-C and/or non-HDL-C levels to guide appropriate treatment. The guidelines also state that adherence to lifestyle and to statin therapy should be re-emphasized before considering the addition of a non-statin drug (Stone et al., 2014). Recent ACC/AHA recommendations on non-statin use do not consider the use of omega-3 fatty acids as they did not include therapies for severe hypertriglyceridemia (Lloyd-Jones et al., 2016; Lloyd-Jones et al., 2017).
- The National Lipid Association recommends omega-3 fatty acids, fibric acid derivatives, or niacin as first-line agents for patients with TG levels of 1000 mg/dL or greater. These agents may also be considered for patients with contraindications for, or intolerance to, statin therapy (Jacobson et al., 2015).
- The Endocrine Society Clinical Practice Guidelines state that omega-3 fatty acids, fibrates, and niacin may be considered as monotherapy or in combination with statins in patients with TG levels that are moderate (200 to 999 mg/dL, based on the Endocrine Society criteria) to severe (1,000 to 1999 mg/dL, based on the Endocrine Society criteria) (Berglund et al., 2012).
Table 1. Medications Included Within Class Review

<table>
<thead>
<tr>
<th>Drug</th>
<th>Manufacturer</th>
<th>FDA Approval Date</th>
<th>Generic Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPANOVA (omega-3-carboxylic acids capsule)</td>
<td>AstraZeneca</td>
<td>05/05/2014</td>
<td>-</td>
</tr>
<tr>
<td>LOVAZA (omega-3-acid ethyl esters capsule)</td>
<td>GlaxoSmithKline</td>
<td>11/10/2004</td>
<td>✓</td>
</tr>
<tr>
<td>OMTRYG (omega-3-acid ethyl esters Type A capsule)</td>
<td>Trygg Pharma, Inc.</td>
<td>04/23/2014</td>
<td>-*</td>
</tr>
<tr>
<td>TRIKLO (omega-3-acid ethyl esters capsule)</td>
<td>Key Therapeutics, LLC</td>
<td>08/08/2017</td>
<td>✓ **</td>
</tr>
<tr>
<td>VASCEPA (icosapent ethyl capsule)</td>
<td>Amarin Pharma, Inc.</td>
<td>07/26/2012</td>
<td>-</td>
</tr>
</tbody>
</table>

*OMTRYG was FDA-approved in 2014, but current availability of the product is unclear.
**Branded generic for LOVAZA.
(Drugs@FDA, 2017; Facts and Comparisons, 2017; Clinical Pharmacology, 2017; TRIKLO prescribing information, 2017)

INDICATIONS

Table 2. FDA-Approved Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>EPANOVA (omega-3-carboxylic acids)</th>
<th>LOVAZA (omega-3-acid ethyl esters)</th>
<th>TRIKLO</th>
<th>OMTRYG</th>
<th>VASCEPA (icosapent ethyl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjunctive treatment to diet to reduce TG levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>


Information on indications, mechanism of action, pharmacokinetics, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

- There are currently no head-to-head efficacy trials comparing EPANOVA (omega-3-carboxylic acids), LOVAZA and OMTRYG (omega-3-acid ethyl esters), or VASCEPA (icosapent ethyl). One study compared the effects of an acylglycerol omega-3 formulation, which is often available in non-prescription omega-3 supplements to LOVAZA. In this double-blind trial in patients with TG concentrations of 150 to 500 mg/dL, 120 patients were randomized to 5563 mg acylglycerol omega-3 daily, LOVAZA 4 g daily, or placebo (olive oil). Both omega-3 groups had decreased TG concentrations compared with placebo (P<0.001), but no difference was found between active treatments (28% reduction with acylglycerol omega-3 and 22% with LOVAZA; P=0.785). Unfortunately, patients included in this study had mild to moderate elevations in TG at baseline, and it is unclear if the acylglycerol omega-3 formulation would have similar results in patients with severe hypertriglyceridemia (Hedengran et al, 2015).

- EpanoVa fOr Lowering Very high triglycerideEs (EVOLVE) was a 12-week, double-blind, placebo (olive oil)-controlled, randomized trial that evaluated the safety and lipid-altering efficacy of EPANOVA (omega-3-carboxylic acids) in 399 adult patients with average serum TG concentrations of ≥500 mg/dL but <2,000 mg/dL at screening (one and two weeks before random assignment). Patients were either treatment-naive for dyslipidemia or using a stable (for at least six weeks before the first qualifying lipid measurement) dosage of a statin, cholesterol absorption inhibitor (CAI), or their combination. They were randomized to one of four treatment groups: placebo (olive oil) (n=99), or EPANOVA 2 g (n=100), 3 g (n=101), or 4 g (n=99). The EPANOVA 3 g group demonstrated a lower TG reduction than the other two active treatment groups. Treatment with EPANOVA 2 g and EPANOVA 4 g compared to placebo led to statistically significant reductions in fasting TG levels (P<0.01 and P<0.001, respectively) and in non-HDL-C levels (P<0.05 and
Data as of November 10, 2017 LK-U/MG-U/DRB

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The Risk and Prevention Study compared LOVAZA (omega-3-acid ethyl esters) to placebo in patients evaluated to be at a high cardiovascular risk and demonstrated no difference in the rate of death, nonfatal MI, and nonfatal stroke. The primary end point occurred in 1,478 of 12,505 patients included in the analysis (11.8%), of whom 733 of 6,239 (11.7%) had received omega-3 PUFA and 745 of 6,266 (11.9%) had received placebo (hazard ratio [HR], 0.97; 95% CI, 0.88 to 1.08; P=0.58) (Risk and Prevention Study Collaborative Group et al, 2013).

A randomized controlled trial comparing LOVAZA (omega-3-acid ethyl esters) to placebo in patients with confirmed symptomatic paroxysmal atrial fibrillation (AF) that required cardioversion, who had at least two episodes of AF in the six months before randomization, or both, demonstrated no significant difference in the rate of recurrence of symptomatic AF. At 12 months, 56 of 297 participants (18.9%) in the placebo group and 69 of 289 participants (24%) in the omega-3 PUFA group had a recurrent symptomatic AF (HR, 1.28; 95% CI, 0.90 to 1.83; P=0.17) (Macchia et al, 2013).

There are no published trials evaluating VASCEPA (icosapent ethyl) as an adjunctive therapy to treat hypercholesterolemia or evaluating the cardiovascular outcomes with this agent. However, a formulation of icosapent ethyl has been marketed in Japan since 1994 under the trade name EPADEL® (ethyl-eicosapentaenoic acid, the active metabolite of icosapent ethyl). Published studies have evaluated this formulation as an adjunctive therapy with estriol and statins and the cardiovascular outcomes of this agent.

In a prospective observational, 48-week trial, EPADEL (ethyl-eicosapentaenoic acid) 1,800 mg daily added to estriol 2 mg daily was compared to estriol 2 mg daily alone. TC decreased significantly from baseline in both groups. Serum levels of TGs decreased significantly from 194.5 to 141.5 mg/dL (-27.2%; P=0.001) in the study group but increased slightly from 192.9 to 207.4 mg/dL (+7.5%) in the control group at week 48 in the women whose level of TGs was not <150 mg/dL (Kurabayashi et al, 2000).

In an open-label trial, 900 to 1,800 mg/day of EPADEL (ethyl-eicosapentaenoic acid) was administered to patients with hyperlipidemia who had been treated with statins for an average of 30 months. Serum TC and TG concentrations were significantly decreased three months after the administration of EPADEL (ethyl-eicosapentaenoic acid) (from 5.63 to 5.02 mmol/L, P<0.05; from 2.07 to 1.08 mmol/L; P<0.01, respectively) (Nakamura et al, 1999).

In the Japan Eicosapentaenoic Acid Lipid Intervention Study (JELIS), a prospective, open label, blinded endpoint trial, 18,645 patients were randomly assigned to receive either 1,800 mg of EPADEL (ethyl-eicosapentaenoic acid) daily with a statin or statin therapy alone. The primary endpoint was any major coronary event, including sudden cardiac death, fatal and non-fatal MI, and other non-fatal events including unstable angina pectoris, angioplasty, stenting, or coronary artery bypass grafting. At mean follow-up of 4.6 years, the primary endpoint occurred less frequently in the EPADEL (ethyl-eicosapentaenoic acid) group compared to the control group (262 [2.8%] vs. 324 [3.5%], respectively; RR=0.19; P=0.011) (Yokoyama et al, 2007).

Seven sub-analyses have been published of the JELIS study.

The reduction in cardiovascular risk was greater in the EPADEL (ethyl-eicosapentaenoic acid) group compared to the control group in patients unable to attain LDL-C and/or high density lipoprotein cholesterol (HDL-C) goals (-38% reduced risk; P=0.007), those with peripheral artery disease (HR, 0.44, 95% CI, 0.19 to 0.97; P=0.041), those with preexisting coronary artery disease (CAD) and a TC ≥250 mg/dL (8.7% vs. 10.7%, respectively; HR, 0.77, 95% CI, 0.63 to 0.96; P=0.017) and regardless of the number of cardiovascular risk factors (hypercholesterolemia, obesity, high TG or low HDL-C, diabetes, and hypertension) (P<0.05 for all comparisons) (Ishikawa et al, 2010; Matsuzaki et al, 2009; Saito et al, 2008, Sasaki et al, 2012).

The use of EPADEL (ethyl-eicosapentaenoic acid) was associated with a significantly greater decrease in CAD compared to the control group in patients with impaired glucose metabolism, but not normoglycemic patients (P=0.048 and P=0.062, respectively) (Oikawa et al, 2009).

Adherence to ≥80% of the medication regimen was associated with a decreased incidence of cardiovascular endpoints compared to those exhibiting <80% adherence to study medications (P=0.041) (Origasa et al, 2010).

The incidence of secondary stroke was lower in the EPADEL (ethyl-eicosapentaenoic acid) group compared to the control group (6.8 vs 10.5%, respectively; HR, 0.80; 95% CI, 0.64 to 0.997; P=0.047); however, there was no difference between groups in the incidence of primary stroke (1.5 vs 1.3%, respectively; HR, 1.08; 95% CI, 0.95 to 1.22; P=0.244) (Tanaka et al, 2008).
The authors of a Cochrane systematic review that examined the effects of omega-3 fatty acids on the prevention and treatment of CVD concluded that it is unclear whether dietary or supplemental omega-3 fats reduce or increase total mortality or combined cardiovascular events in people with, or at risk of, CVD or in the general population (Hooper et al, 2004).

The 2013 ACC/AHA guidelines emphasize adherence to lifestyle and to statin therapy before considering the addition of a nonstatin drug (Stone et al, 2013). Other guidelines suggest a potential role for other lipid-lowering therapies when treating hypertriglyceridemia including fibric acid derivatives, niacin, and omega-3 fatty acids (Jellinger et al, 2012; Jacobson et al, 2015).

**SAFETY SUMMARY**

- Omega-3 fatty acids have precautions for use in patients with hepatic impairment and fish allergy. LOVAZA, TRIKLO, OMTRYG (omega-3 acid ethyl esters) and EPANOVA (omega-3-carboxylic acids) may be associated with increases in LDL-C. Additionally, LOVAZA, TRIKLO, and OMTRYG have a possible association with atrial fibrillation or flutter.
- The most common adverse reactions associated with LOVAZA, TRIKLO, and OMTRYG (incidence >3% and greater than placebo) were eructation, dyspepsia, and taste perversion.
- The most common adverse reactions with EPANOVA (incidence ≥ 3% and greater than placebo) were eructation, nausea, diarrhea, and abdominal pain. Additional adverse reactions include vomiting, flatulence, and taste perversion.
- The most common adverse reaction associated with VASCEPA (incidence >2% and greater than placebo) was arthralgia.

**DOSING AND ADMINISTRATION**

**Table 3. Dosing and Administration**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Form: Strength</th>
<th>Usual Recommended Dose</th>
<th>Other Dosing Considerations</th>
<th>Administration Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPANOVA (omega-3-carboxylic acids)</td>
<td>Coated soft gelatin capsule: 1 g</td>
<td>Adjunct to diet to reduce TG levels in adult patients with severe hypertriglyceridemia: 2 g or 4 g once daily depending on individual patient response and tolerability</td>
<td>Assess TG levels carefully before initiating therapy. Identify other causes (e.g., diabetes mellitus, hypothyroidism, or medications) of high TG levels and manage as appropriate. Patients should be placed on an appropriate lipid-lowering diet prior to receiving treatment and should continue diet during therapy.</td>
<td>In clinical trials, this agent was administered without regard to meals. Swallow capsules whole. Do not break open, crush, dissolve, or chew. Gelatin source: porcine</td>
</tr>
<tr>
<td>LOVAZA and TRIKLO (omega-3-acid ethyl esters)</td>
<td>Soft-gelatin capsule: 1 g</td>
<td>Adjunct to diet to reduce TG levels in adult patients with severe hypertriglyceridemia: 4 g/day administered once daily or in two divided doses</td>
<td>Assess TG levels carefully before initiating therapy. Identify other causes (e.g., diabetes mellitus, hypothyroidism, or medications) of high TG levels and manage as appropriate. Patients should be placed on an appropriate lipid-lowering diet prior to receiving treatment and should continue diet during therapy.</td>
<td>In clinical trials, this agent was administered with meals. Swallow capsules whole. Do not break open, crush, dissolve, or chew.</td>
</tr>
<tr>
<td>OMTRYG (omega-3-acid ethyl esters)</td>
<td>Soft-gelatin capsule: 1.2 g (containing</td>
<td>Adjunct to diet to reduce TG levels in adult patients with severe</td>
<td>Assess TG levels carefully before initiating therapy. Identify other causes (e.g.,</td>
<td>Should be administered with food.</td>
</tr>
<tr>
<td>Drug</td>
<td>Dosage Form: Strength</td>
<td>Usual Recommended Dose</td>
<td>Other Dosing Considerations</td>
<td>Administration Considerations</td>
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<tr>
<td>≥900 mg ethyl esters of omega-3 fatty acids</td>
<td>(≥500 mg/dL) hypertriglyceridemia: 4 capsules/day administered once daily or in two divided doses</td>
<td>diabetes mellitus, hypothyroidism, or medications of high TG levels and manage as appropriate. Patients should be placed on an appropriate lipid-lowering diet prior to receiving treatment and should continue diet during therapy.</td>
<td>Swallow capsules whole. Do not break open, crush, dissolve, or chew.</td>
<td></td>
</tr>
<tr>
<td>VASCEPA (icosapent ethyl)</td>
<td>Soft-gelatin capsule: 0.5 g, 1 g</td>
<td>Adjunct to diet to reduce TG levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia: 4 g/day administered in two divided doses</td>
<td>Assess TG levels carefully before initiating therapy. Identify other causes (e.g., diabetes mellitus, hypothyroidism, or medications) of high TG levels and manage as appropriate. Patients should be placed on an appropriate lipid-lowering diet prior to receiving treatment and should continue diet during therapy.</td>
<td>Should be administered with food. Swallow capsules whole. Do not break open, crush, dissolve, or chew.</td>
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</table>

**SPECIAL POPULATIONS**

Table 4. Special Populations

<table>
<thead>
<tr>
<th>Drug</th>
<th>Population and Precaution</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPANOVA (omega-3-carboxylic acids)</td>
<td>Clinical trials did not include sufficient numbers of patients ≥65 years of age to determine if they have a different response than younger patients. In general, therapy should be initiated at the lower end of the dosing range for elderly patients. Safety and efficacy have not been established. Safety and efficacy have not been established. Safety and efficacy have not been established. Unclassified†</td>
</tr>
<tr>
<td></td>
<td>Safety and efficacy have not been established.</td>
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<tr>
<td></td>
<td>Safety and efficacy have not been established.</td>
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<tr>
<td></td>
<td>Safety and efficacy have not been established.</td>
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<td></td>
<td>No studies in pregnant women: data insufficient to inform risk.</td>
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<td></td>
<td>No information regarding presence in human breast milk or effects on breast-fed infants.</td>
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<tr>
<td></td>
<td>Limited studies show that omega-3 fatty acids are present in human milk at levels higher than plasma concentrations.</td>
</tr>
<tr>
<td>Drug</td>
<td>Population and Precaution</td>
</tr>
<tr>
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</tr>
<tr>
<td><strong>LOVAZA, TRIKLO, and OMTRYG (omega-3-acid ethyl esters)</strong></td>
<td><strong>Elderly</strong></td>
</tr>
<tr>
<td></td>
<td>The efficacy and safety profile among those ≥60 years of age did not appear to differ from the efficacy and safety profile observed in younger patients.</td>
</tr>
<tr>
<td></td>
<td>Safety and efficacy have not been established.</td>
</tr>
<tr>
<td><strong>VASCEPA (icosapent ethyl)</strong></td>
<td>No overall differences in safety or effectiveness were observed between subjects ≥65 years of age and younger subjects.</td>
</tr>
<tr>
<td></td>
<td>Safety and efficacy have not been established.</td>
</tr>
</tbody>
</table>

*Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
†In accordance with the FDA’s Pregnancy and Lactation Labeling Rule (PLLR), this product is not currently assigned a Pregnancy Category. Consult product prescribing information for details.

**CONCLUSION**

- Prescription omega-3 fatty acids are approved by the FDA for the treatment of severe hypertriglyceridemia. There is a generic formulation of LOVAZA (omega-3-acid ethyl esters) currently available, as well as a branded generic product (TRIKLO).
- In patients with an elevated TG level (≥500 mg/dL), a fibric acid derivative or niacin should be initiated before LDL-C lowering therapy to prevent pancreatitis. Omega-3-acid fatty acids represent an alternative to fibric acid derivatives and niacin for the treatment of hypertriglyceridemia. Select clinical trials suggest that relatively high doses of omega-3-fatty acids, in the form of fish, fish oils or high-linolenic acid oils, will reduce the risk for major coronary events in persons with established coronary heart disease; however, the overall body of literature does not offer convincing evidence that fish oil supplements are beneficial for preventing cardiovascular disease or improving outcomes.
- Clinical trials have demonstrated that prescription omega-3 acid ethyl esters can effectively lower TGs, as well as positively impact other lipid/lipoprotein parameters when used as monotherapy or in combination with fenofibrate or statins.
- In select placebo-controlled trials, both LOVAZA and OMTRYG (omega-3-acid ethyl esters) and EPANOVA (omega-3 carboxylic acids) were associated with an increase in LDL-C levels from baseline compared to placebo.
- In placebo-controlled trials, VASCEPA (icosapent ethyl) was not associated with an increase in LDL-C levels from baseline compared to placebo.
- Select cardiovascular outcomes studies have suggested a decrease in cardiovascular outcomes with LOVAZA (omega-3 acid ethyl esters) and VASCEPA (icosapent ethyl); however, certain trials have demonstrated no benefit compared to a control group.
- EPANOVA (omega-3-carboxylic acids) is the first FDA-approved prescription omega-3 in free fatty acid form, which produces higher bioavailability than esterified forms. Unlike the other prescription omega-3 fatty acids, EPANOVA can be taken without regard to meals. It does have a similar safety profile as the existing available products.
- The 2013 ACC/AHA guidelines emphasize adherence to lifestyle and to statin therapy before considering the addition of a nonstatin drug. When EPA and/or DHA are used to treat severe hypertriglyceridemia, it is reasonable to evaluate the patient for gastrointestinal disturbances, skin changes, and bleeding (Stone et al, 2013).
Table 5. Advantages and Disadvantages of Omega-3 Fatty Acids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPANOVA (omega-3-carboxylic acids)</td>
<td>• First FDA-approved prescription omega-3 in free fatty acid form</td>
<td>• May be associated with an increase in LDL-C levels</td>
</tr>
<tr>
<td></td>
<td>• Can be taken with or without food</td>
<td>• The effects of the agent on the risk of pancreatitis or cardiovascular</td>
</tr>
<tr>
<td></td>
<td>• Dosing option may be as few as two capsules once daily</td>
<td>mortality and morbidity in patients with severe hypertriglyceridemia have</td>
</tr>
<tr>
<td></td>
<td></td>
<td>not been determined.</td>
</tr>
<tr>
<td>LOVAZA, TRIKLO, and OMTRYG (omega-3-acid ethyl esters)</td>
<td>• Clinical trials have established that this agent is associated with a decrease in TG levels and select other lipid parameters.</td>
<td>• May be associated with an increase in LDL-C levels</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The effects of the agent on the risk of pancreatitis or cardiovascular</td>
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<tr>
<td></td>
<td></td>
<td>mortality and morbidity in patients with severe hypertriglyceridemia have</td>
</tr>
<tr>
<td></td>
<td></td>
<td>not been determined.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The absorption is greater when given with high-fat high-calorie meals.</td>
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<tr>
<td></td>
<td></td>
<td>Since many patients with hypertriglyceridemia are advised to stick to a low-fat diet, this could negatively affect absorption.</td>
</tr>
<tr>
<td>VASCEPA (icosapent ethyl)</td>
<td>• Clinical trials have established that this agent is associated with a decrease in TG levels and select other lipid parameters.</td>
<td>• The effects of the agent on the risk of pancreatitis or cardiovascular</td>
</tr>
<tr>
<td></td>
<td>• May not be associated with an increase in LDL-C levels</td>
<td>mortality and morbidity in patients with severe hypertriglyceridemia have</td>
</tr>
<tr>
<td></td>
<td></td>
<td>not been determined.</td>
</tr>
</tbody>
</table>

REFERENCES

- Hedengran A, Szczes PB, Dyerberg J, Harris WS, Stender S. n-3 PUFA esterified to glycerol or as ethyl esters reduce non-fasting plasma triacylglycerol in subjects with hypertriglyceridemia: a randomized trial. Lipids. 2015;50(2):165-175.

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• LOVaza prescribing information. GlaxoSmithKline, Research Triangle Park, NC. September 2015.


• TRIKLO prescribing information. Key Therapeutics, LLC. Flowood, MS. August 2017.


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