TITLE

COMPOSITIONS AND METHODS FOR LOWERING TRIGLYCERIDES WITHOUT RAISING LDL-C LEVELS IN A SUBJECT ON CONCOMITANT STATIN THERAPY

BACKGROUND

[0001] Cardiovascular disease is one of the leading causes of death in the United States and most European countries. It is estimated that over 70 million people in the United States alone suffer from a cardiovascular disease or disorder including but not limited to high blood pressure, coronary heart disease, dislipidemia, congestive heart failure and stroke.

SUMMARY

[0002] In one aspect, the present disclosure refers to use of ethyl eicosapentaenoate in the manufacture of one or more capsules for lowering triglycerides and serum LDL-C in a subject having mixed dyslipidemia on stable statin therapy having baseline fasting triglycerides of 200 mg/dl to 500 mg/dl, wherein the capsules comprise not more than 4% docosahexaenoic acid or its esters, by weight of all fatty acids, and are to be administered to provide 4 g per day of the ethyl eicosapentaenoate to the subject for a period of at least 12 weeks. In another aspect, the present disclosure refers to use of ethyl eicosapentaenoate in the manufacture of a medicament for lowering triglycerides and serum LDL-C in a subject on stable statin therapy having baseline fasting triglycerides of 200 mg/dl to 500 mg/dl and an LDL-C level of 40 mg/dl to 100 mg/dl, wherein the medicament comprises not more than 4% docosahexaenoic acid or its esters, by weight of all fatty acids, and is to be orally administered to the subject to provide 4 g of the ethyl eicosapentaenoate per day for a period of at least 12 weeks. In various examples, the present disclosure provides pharmaceutical compositions and methods of using such compositions to treat and/or prevent cardiovascular-related diseases. In one example, the subject is on concomitant statin therapy. In another example, the subject on statin therapy has a baseline fasting serum triglyceride level of about 200 mg/dL to about 500 mg/dL.

[0003] In one example, the disclosure provides a method of lowering triglycerides in a subject on stable statin therapy having baseline fasting triglycerides of about 200 mg/dl to about 500 mg/dl, the method comprising administering to the subject a pharmaceutical composition comprising polyunsaturated fatty acids, for example about 1 g to about 4 g of EPA per day, wherein upon administering the composition to the subject daily for a period of 12 weeks the subject exhibits at least 5% lower fasting triglycerides than a control subject maintained on stable statin therapy (optionally with placebo matching the EPA) without concomitant EPA for a period of 12 weeks wherein the control subject also has baseline fasting triglycerides of about 200 mg/dl to about 500 mg/dl. In another example, upon administering the composition to the subject daily for a period of 12 weeks the subject exhibits no serum LDL-C increase, no statistically significant serum LDL-C increase, a serum LDL-C decrease, or the subject is statistically non-inferior to the control subjects (statin plus optional placebo) in regard to serum LDL-C elevation).

[0004] These and other examples of the present disclosure will be disclosed in further detail herein below.

CLAIMS

What is claimed is:

1. Use of ethyl eicosapentaenoate in the manufacture of one or more capsules for lowering triglycerides and serum LDL-C in a subject having mixed dyslipidemia on stable statin therapy having baseline fasting triglycerides of 200 mg/dl to 500 mg/dl, wherein the capsules comprise not more than 4% docosahexaenoic acid or its esters, by weight of all fatty acids, and are to be administered to provide 4 g per day of the ethyl eicosapentaenoate to the subject for a period of at least 12 weeks.

2. The use of claim 1 wherein the subject has coronary heart disease or a coronary heart disease risk equivalent.

3. The use of claim 2 wherein the subject has an LDL-C level of 40 mg/dl to 100 mg/dl prior to the one or more capsules being administered.

4. The use of claim 1 wherein an LDL-C level is reduced in the subject after a period of at least 12 weeks.

5. The use of claim 4 wherein the subject exhibits a reduction in one or more of: non-HDL-C, VLDL-C, Lp-PLA2, apolipoprotein B, total cholesterol, or VLDL-TG.

6. The use of claim 1 wherein the subject exhibits a reduction in one or more of: non-HDL-C, VLDL-C, Lp-PLA2, apolipoprotein B, total cholesterol, or VLDL-TG.

7. The use of claim 1 wherein the one or more capsules each comprise about 1 g of the ethyl eicosapentaenoate.

8. Use of ethyl eicosapentaenoate in the manufacture of a medicament for lowering triglycerides and serum LDL-C in a subject on stable statin therapy having baseline fasting triglycerides of 200 mg/dl to 500 mg/dl and an LDL-C level of 40 mg/dl to 100 mg/dl, wherein the medicament comprises not more than 4% docosahexaenoic acid or its esters, by weight of all

fatty acids, and is to be orally administered to the subject to provide 4 g of the ethyl eicosapentaenoate per day for a period of at least 12 weeks.

9. The use of claim 8 wherein the subject has coronary heart disease or a coronary heart disease risk equivalent.

10. The use of claim 9 wherein the subject has an LDL-C level of 40 mg/dl to 100 mg/dl prior to the medicament being administered.

11. The use of claim 10 wherein the subject has mixed dyslipidemia.

12. The use of claim 11 wherein LDL-C is reduced in the subject after the period of at least 4 weeks.

13. The use of claim 12 wherein the subject exhibits a reduction in one or more of: non-HDL-C, VLDL-C, Lp-PLA2, apolipoprotein B, total cholesterol, or VLDL-TG.