IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMARIN PHARMA, INC., AMARIN PHARMACEUTICALS IRELAND LIMITED, MOCHIDA PHARMACEUTICAL CO., LTD., Plaintiffs, v. HIKMA PHARMACEUTICALS USA INC., HIKMA PHARMACEUTICALS PLC, AND HEALTH NET, LLC Defendants.	C.A. No. 20-1630-RGA **JURY TRIAL DEMANDED**

FIRST AMENDED COMPLAINT FOR PATENT INFRINGEMENT AND DEMAND FOR JURY TRIAL

Plaintiffs Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited ("Amarin") and Mochida Pharmaceutical Co., Ltd. ("Mochida") (collectively, "Plaintiffs"), by their attorneys, hereby allege as follows:

THE NATURE OF THE ACTION

1. This is an action for infringement of U.S. Patent Nos. 9,700,537 ("the '537 patent"), 8,642,077 (the "'077 patent"), and 10,568,861 (the "'861 patent") (collectively, the "Asserted Patents") under the Patent Laws of the United States, 35 U.S.C. § 100 et seq., including § 271(b). In violation of these laws, the Hikma Defendants are marketing their generic version of Amarin's ground-breaking VASCEPA® product to reduce the risk of cardiovascular events such as heart attack and stroke ("cardiovascular risk reduction"), and Health Net is inducing pharmacies to dispense, and patients to use it, for that purpose. VASCEPA® is the first and only innovative

omega-3 acid-based product approved for cardiovascular risk reduction by the United States Food and Drug Administration.

THE PARTIES

2. Amarin Pharma, Inc. is a company organized under the laws of Delaware with its principal place of business at 440 Route 22, Suite 330, Bridgewater, NJ 08870.

3. Amarin Pharmaceuticals Ireland Limited is a company incorporated under the laws of Ireland with registered offices at 88 Harcourt Street, Dublin 2, Dublin, Ireland.

4. Mochida Pharmaceutical Co., Ltd. is a company incorporated under the laws of Japan with its principal place of business at 1-1, Ichigayahonmuracho, Shinjuku-ku, Tokyo 162-0845, Japan.

5. On information and belief, Defendant Hikma Pharmaceuticals USA Inc. is a corporation organized and existing under the laws of Delaware with its principal place of business at 246 Industrial Way West, Eatontown, NJ 07724.

6. On information and belief, Defendant Hikma Pharmaceuticals PLC is a corporation organized and existing under the laws of the United Kingdom with its principal place of business at 1 New Burlington Place, London W1S 2HR.

7. Upon information and belief, Hikma Pharmaceuticals USA Inc. is a wholly-owned subsidiary of Hikma Pharmaceuticals PLC.

8. Upon information and belief, Hikma Pharmaceuticals USA Inc. acts at the direction, and for the benefit, of Hikma Pharmaceuticals PLC, and is controlled and/or dominated by Hikma Pharmaceuticals PLC. Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC are hereinafter referred to together as "the Hikma Defendants" or "Hikma."

9. Upon information and belief, the Hikma Defendants collaborate with respect to the development, regulatory approval, marketing, sale, and/or distribution of pharmaceutical products. On further information and belief, the Hikma Defendants are agents of each other and/or operate in concert as integrated parts of the same business group, and enter into agreements with each other that are nearer than arm's length.

10. Upon information and belief, Hikma Pharmaceuticals USA Inc. is the current owner of ANDA No. 209457 for 1g and 0.5 g icosapent ethyl capsules purportedly bioequivalent to VASCEPA®.

11. Upon information and belief, on May 21, 2020, FDA granted final approval for the Hikma Defendants' 1g icosapent ethyl capsules under ANDA No. 209457.

12. Attached hereto as Exhibit A is a press release issued by Hikma Pharmaceuticals PLC on or about May 22, 2020 announcing that "Hikma Pharmaceuticals USA Inc. has received approval from the US Food and Drug Administration (FDA) for its Icosapent Ethyl Capsules, 1 gm, the generic equivalent to Vascepa®."

13. Attached hereto as Exhibit N is a press release issued by Hikma Pharmaceuticals PLC on or about November 5, 2020 announcing the launch of Hikma's icosapent ethyl capsules. On information and belief, on November 5, 2020, Hikma launched and began offering for sale and/or selling its generic icosapent ethyl capsules in the United States, including this jurisdiction.

14. Upon information and belief, the Hikma Defendants act collaboratively to commercially manufacture, market, distribute, offer for sale, and/or sell Hikma's icosapent ethyl capsules in the United States, including this jurisdiction.

15. On information and belief, Health Net, LLC is a limited liability company organized and existing under the laws of the State of Delaware with a principal place of business at 21281

Burbank Boulevard in Woodland Hills, California 91367. Health Net, LLC is referred to herein as "Health Net" and collectively with the Hikma Defendants as "Defendants."

16. On information and belief, Health Net, on its own and through its various subsidiaries, provides insurance coverage for patients in the United States.

JURISDICTION AND VENUE

17. This Court has subject matter jurisdiction over the action under 28 U.S.C. §§ 1331 and 1338(a).

18. This Court has personal jurisdiction over Hikma Pharmaceuticals USA Inc. because it is incorporated in Delaware and thus is present in and resides in this District, and because Hikma Pharmaceuticals USA Inc. is doing business in this District and has thus purposefully availed itself to the privileges of conducting business in Delaware.

19. Venue is proper in this District over Hikma Pharmaceuticals USA, Inc. under 28 U.S.C. § 1400(b).

20. This Court has personal jurisdiction over Hikma Pharmaceuticals PLC because, on information and belief, it manufactures, imports, offers for sale, and sells pharmaceutical drugs that are sold in the United States, including in Delaware, and derives substantial income therefrom.

21. In the alternative, this Court may exercise personal jurisdiction over Hikma Pharmaceuticals PLC pursuant to Fed. R. Civ. P. 4(k)(2) because (a) Plaintiffs' claims arise under federal law; (b) Hikma Pharmaceuticals PLC is a foreign company not subject to personal jurisdiction in the courts in any state, and (c) Hikma Pharmaceuticals PLC has sufficient contacts with the United States as a whole, including but not limited to marketing and/or selling generic pharmaceutical products that are distributed and sold throughout the United States, such that this Court's exercise of jurisdiction over Hikma Pharmaceuticals PLC satisfies due process.

22. Venue is proper in this District with respect to Hikma Pharmaceuticals PLC pursuant to 28 U.S.C. § 1391(c)(3) because it is not resident in the United States.

23. This Court has personal jurisdiction over Health Net because it is organized under the law of Delaware and thus is present in and resides in this District.

24. Venue is proper in this District over Health Net under 28 U.S.C. § 1400(b).

FACTUAL BACKGROUND

A. VASCEPA®, REDUCE-IT, JELIS and EPA's Reduction of Cardiovascular Risk

25. The three types of omega−3 fatty acids involved in human physiology are α-linolenic acid (ALA), found in plant oils, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), both commonly found in marine (fish) oils.

26. Amarin and Mochida are recognized worldwide as the leading innovation-driven companies committed to the research and development of EPA-based drug products to treat the needs of millions of patients who are at risk of cardiovascular disease.

27. Mochida developed and markets a prescription pure EPA drug product, Epadel, in Japan.

28. Amarin developed and markets VASCEPA®, a prescription drug that contains pure EPA, in the United States.

29. Amarin conducted a series of clinical trials to support FDA approval of VASCEPA®.

30. In the MARINE trial that led to VASCEPA®'s first approval, VASCEPA® was found to lower triglycerides in patients with severe hypertriglyceridemia (≥500 mg/dL) without raising bad cholesterol, or LDL-C, levels. Upon FDA approval in 2012, VASCEPA® became the first (and still only) approved medication for treating severe hypertriglyceridemia that does not raise LDL-C.

31. After that approval to treat severe hypertriglyceridemia, Amarin continued its clinical work towards its primary goal, approval of VASCEPA® for use in cardiovascular risk reduction. Based on an agreed protocol with the FDA, Amarin had conducted a clinical trial known as ANCHOR, in which Amarin examined VASCEPA® as an add-on to statin therapy in patients with persistent high (≥200 mg/dL and <500 mg/dL) triglycerides. As agreed with FDA, Amarin evaluated VASCEPA®'s effect on cardiovascular risk reduction based on triglyceride level lowering as a surrogate, or substitute, for cardiovascular risk reduction while awaiting the results of Amarin's REDUCE-IT trial.

32. While ANCHOR met its clinical endpoints, including the exploratory endpoint of median placebo-adjusted percent change in high-sensitivity C reactive protein (hs-CRP), *see* Ex. U (Ballantyne), FDA's view on the use of triglyceride levels as a surrogate for cardiovascular risk changed. Ex. BB. FDA identified several clinical trials where other therapies, including other omega-3 based therapies, lowered triglyceride levels in this patient population but did not show an actual reduction in cardiovascular risk. The trials failing to show a cardiovascular risk reduction included ACCORD-Lipid, AIM-HIGH, and HPS2-THRIVE.

33. Accordingly, Amarin proceeded to complete REDUCE-IT, a trial in which the effects of VASCEPA® on cardiovascular risk reduction were evaluated directly. The REDUCE-IT study was completed by Amarin at great cost. In REDUCE-IT, Amarin followed more than 8000 patients over a median of five years and evaluated the effectiveness of VASCEPA® as an add-on to statin therapy in reducing major cardiovascular events in patients with persistent elevated triglycerides. *See* Ex. V (Bhatt).

34. The results of REDUCE-IT, first announced in 2018, *see* Ex. H, were hailed as one of the most important developments in the prevention and treatment of cardiovascular disease since

statins. Compared to statins alone on top of other contemporaneous medical therapy, VASCEPA® showed a 25% reduction in major cardiovascular events such as cardiovascular death, myocardial infarction, and stroke. Based on those results, in December 2019, FDA approved VASCEPA® for a second indication as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease. Ex. I. Similar to the ANCHOR results, a reduction in hs-CRP was observed in REDUCE-IT which may in part explain the cardiovascular risk benefit. *See* Ex. V (Bhatt) at 20. This is consistent with the investigators in the ANCHOR trial, who stated that one of the potential explanations for increased cardiovascular risk might be inflammation and VASCEPA® showed a 22% reduction of hs-CRP in the mixed dyslipidemia population studied in ANCHOR. *See* Ex. U (Ballantyne); *see also* Exhibit O at col. 18, l. 11-12.

35. In a press release about this additional approval, FDA recognized that "VASCEPA is the first FDA-approved drug to reduce cardiovascular risk among patients with elevated triglyceride levels as an add-on to maximally tolerated statin therapy." Ex. J. The results of REDUCE-IT were met with widespread enthusiasm and surprise in the field and have been hailed as a "game changer" in medicine. Ex. Y; Ex. Z.

36. Amarin's work in the MARINE, ANCHOR, and REDUCE-IT clinical trials was preceded by other work done by Mochida, in Japan. In the late 1990s and early 2000s, Mochida sponsored a cardiovascular outcomes trial with Epadel in Japan, called JELIS (Japanese EPA Lipid Intervention Study). JELIS was the world's first large-scale randomized controlled cardiovascular outcomes trial of a prescription pure EPA drug product. The JELIS results reported that pure EPA

suppressed coronary artery disease in Japanese hypercholesterolemic patients who routinely consume a large amount of EPA and DHA (another poly unsaturated fatty acid) from fish oil in their diet.

37. A further statistical analysis of JELIS was undertaken to assess the effect of EPA on patients with a particular profile of risk factors for coronary artery disease, and reported beneficial effects of the drug in further reducing cardiovascular events in statin-treated, hypercholesterolemic Japanese patients.

38. Those effects are published in Saito et al., titled, "Effects of EPA on coronary artery disease in hypercholesterolemic patients with multiple risk factors: Sub-analysis of primary prevention cases from the Japan EPA Lipid Intervention Study (JELIS), 200 Atherosclerosis 135-400 (2008) [hereinafter, the "Saito Article"]. The Saito Article is attached hereto as Exhibit B.

39. The Saito Article reports on a statistical analysis of patients studied in the JELIS trial who had no history of coronary artery disease (i.e., the patients had not previously had a cardiovascular event). Ex. B (Saito) at § 2.1. The primary endpoint was major coronary events (MCE): sudden cardiac death, fatal myocardial infarction, nonfatal myocardial infarction, unstable angina pectoris including hospitalization for documented ischemic episodes, and angioplasty/stenting or coronary artery bypass grafting. Ex. B (Saito) at § 2.3.

40. The Saito Article reports that the "EPA treatment lowered the risk for MCE for the [studied population] by 53% (HR: 0.47; 95% CI: 0.23-0.98; $P = 0.43$; Fig. 3)." Ex. B (Saito) at 138. By comparison, MCE risk was reduced by 18% in all primary prevention subjects treated in the JELIS clinical study. Ex. B (Saito) at 139.

B. The Asserted Patents

41. On July 11, 2017, the United States Patent and Trademark Office ("USPTO") duly and legally issued the '537 patent, titled "Composition for Preventing the Occurrence of

Cardiovascular Event in Multiple Risk Patient," and naming Mitsuhiro Yokoyama, Hideki Origasa, Masunori Matsuzaki, Yuji Matsuzawa and Yasushi Saito as inventors. A true and correct copy of the '537 patent is attached to this complaint as Exhibit C.

42. The '537 patent is assigned to Mochida Pharmaceutical Co., Ltd.

43. Amarin Pharma, Inc. holds an exclusive license to the '537 patent.

44. The '537 patent reflects and claims the analysis and outcome published in the Saito Article. *See, e.g.*, Ex. C at Example 1 (col. 13, ll. 1 to col. 15, ll. 61 (including the referenced tables and figures)).

45. Claim 1 of the '537 patent recites as follows:

> 1. A method of reducing occurrence of a cardiovascular event in a hypercholesterolemia patient consisting of:
>
> identifying a patient having triglycerides (TG) of at least 150 mg/DL and HDL-C of less than 40 mg/dL in a blood sample taken from the patient as a risk factor of a cardiovascular event, wherein the patient has not previously had a cardiovascular event, and administering ethyl icosapentate in combination with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor,
>
> wherein said 3-hydroxyl-3-methylglutaryl coenzyme A reductase inhibitor is administered to the patient at least one of before, during and after administering the ethyl icosapentate; and
>
> wherein the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor is selected from the group consisting of pravastatin, lovastatin, simvastatin, fluvastatin, atorvastatin, pitavastatin, rosuvastatin, and salts thereof, and
>
> wherein daily dose of the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor are 5 to 60 mg for pravastatin, 2.5 to 60 mg for simvastatin, 10 to 180 mg for fluvastatin sodium, 5 to 120 mg for atorvastatin calcium hydrate, 0.5 to 12 mg for pitavastatin calcium, 1.25 to 60 mg for rosuvastatin calcium, 5 to 160 mg for lovastatin, and 0.075 to 0.9 mg for cerivastatin sodium.

46. On February 4, 2014, the USPTO duly and legally issued the '077, titled "Stable Pharmaceutical Composition and Methods of Using Same," and naming Mehar Manku, Ian Osterloh, Pierre Wicker, Rene Braeckman, and Paresh Soni as inventors. A true and correct copy of the '077 patent is attached to this complaint as Exhibit O.

47. The ’077 patent is assigned to Amarin Pharmaceuticals Ireland Limited.

48. Amarin Pharma, Inc. holds an exclusive license to the ’077 patent.

49. Claims 1 and 8 of the ’077 patent recites as follows:

> 1. A method of reducing triglycerides in a subject with mixed dyslipidemia on statin therapy comprising, administering to the subject a pharmaceutical composition comprising about 2500 mg to 5000 mg per day of ethyl eicosapentaenoate and not more than about 5%, by weight of all fatty acids, docosahexaenoic acid or its esters to effect a reduction in fasting triglyceride levels in the subject.
>
> 8. The method of claim 1 wherein the subject exhibits a reduction in hs-CRP compared to placebo control.

50. On February 25, 2020, the USPTO duly and legally issued the ’861 patent, titled “Methods of reducing the risk of a cardiovascular event in a subject at risk for cardiovascular disease,” and naming Paresh Soni as the inventor. A true and correct copy of the ’861 patent is attached to this complaint as Exhibit P.

51. The ’861 patent is assigned to Amarin Pharmaceuticals Ireland Limited.

52. Amarin Pharma, Inc. holds an exclusive license to the ’861 patent.

53. Claims 1 and 2 of the ’861 patent recite as follows:

> 1. A method of reducing risk of cardiovascular death in a subject with established cardiovascular disease, the method comprising administering to said subject about 4 g of ethyl icosapentate per day for a period effective to reduce risk of cardiovascular death in the subject.
>
> 2. The method of claim 1, wherein the subject has a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL.

C. Amarin’s VASCEPA® Receives FDA Approval for Reducing the Risk of Certain Cardiovascular Events in Patients with High Triglycerides and Low HDL-C Levels Concurrently on Statin Therapy

54. Amarin Pharmaceuticals Ireland Limited is the current holder of NDA No. 202057 for 1 g and 0.5 g icosapent ethyl capsules. Amarin Pharma, Inc. is Amarin Pharmaceuticals Ireland

Limited's agent in the United States for purposes of communicating with the FDA regarding NDA No. 202057. Amarin Pharmaceuticals Ireland Limited and Amarin Pharma, Inc. market both strengths of the approved drug product under the tradename VASCEPA®.

55. A true, correct, and complete copy of the current FDA-approved Prescribing Information for VASCEPA®, covering both the 1 g and 0.5 g strengths, is attached as Exhibit D.

56. VASCEPA® is indicated as (1) an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia (the "Severe Hypertriglyceridemia Indication"), and (2) as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease (the "CV Indication"). Ex. D, § 1.

57. FDA first approved 1 g strength icosapent ethyl capsules, sold under the trade name VASCEPA®, pursuant to NDA No. 202057 on July 26, 2012.

58. A supplement to NDA No. 202057 for the 0.5 g strength of icosapent ethyl capsules was approved on February 16, 2017.

59. From July 26, 2012 through December 12, 2019, the sole indication for which VASCEPA® had received FDA approval was the Severe Hypertriglyceridemia Indication. FDA approval was based, in part, on the MARINE clinical trial and information from that trial is included on the VASCEPA® label. *See* Ex. E (VASCEPA® July 2012 label); Ex. F (VASCEPA® Feb. 2017 label).

60. From 2012 through December 12, 2019, the label for VASCEPA® contained the following limitation of use: "The effect of VASCEPA on cardiovascular mortality and morbidity

in patients with severe hypertriglyceridemia has not been determined" (the "CV Limitation of Use"). *See* Ex. E (VASCEPA® July 2012 label); Ex. F (VASCEPA® Feb. 2017 label). The CV Limitation of Use appeared in three places on the VASCEPA® label during that time period. *See* Ex. E at Highlights of Prescribing Information and Sections 1 and 14; Ex. F (same). The CV Limitation of Use as it appears in the VASCEPA® Label approved by FDA in February 2017 is reproduced below with annotations in red:

HIGHLIGHTS OF PRESCRIBING INFORMATION

VASCEPA® (icosapent ethyl) Capsules, for oral use
Initial U.S. Approval: 2012

These highlights do not include all the information needed to us VASCEPA® safely and effectively. See full prescribing information fo VASCEPA.

----------INDICATIONS AND USAGE----------

VASCEPA is an ethyl ester of eicosapentaenoic acid (EPA) indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:
•The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

•The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined. (1)

Ex. F at Highlights of Prescribing Information.

1 INDICATIONS AND USAGE

VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet and exercise regimen before receiving VASCEPA and should continue this diet and exercise regimen with VASCEPA.

Attempts should be made to control any medical problems such as diabetes mellitus, hypothyroidism, and alcohol intake that may contribute to lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed, if possible, prior to consideration of TG-lowering drug therapy.

Limitations of Use:

The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

Id. § 1.

VASCEPA 4 grams per day reduced median TG, VLDL-C, and Apo B levels from baseline relative to placebo. The reduction in TG observed with VASCEPA was not associated with elevations in LDL-C levels relative to placebo.

The effect of VASCEPA on the risk of pancreatitis in patients with severe hypertriglyceridemia has not been determined.

The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

Id. § 14.

61. The CV Limitation of use appearing on the VASCEPA® label from 2012 through December 12, 2019 was consistent with other products in the therapeutic category, such as LOVAZA®, a combination of ethyl esters of omega 3 fatty acids including EPA. To illustrate, the version of the LOVAZA® label approved by FDA on April 3, 2019 also contained the CV Limitation of Use, as shown below with an annotation in red:

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LOVAZA safely and effectively. See full prescribing information for LOVAZA.

LOVAZA (omega-3-acid ethyl esters capsules), for oral use
Initial U.S. Approval: 2004

----------INDICATIONS AND USAGE----------
LOVAZA is a combination of ethyl esters of omega 3 fatty acids, principally eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia (HTG). (1)

Limitations of Use:
- The effect of LOVAZA on the risk for pancreatitis has not been determined. (1)
- The effect of LOVAZA on cardiovascular mortality and morbidity has not been determined. (1)

Ex. S at Highlights of Prescribing Information.

62. On December 13, 2019, FDA approved VASCEPA® for the CV Indication, based on the results of the REDUCE-IT clinical trial. *See* Ex. G.

63. In conjunction with VASCEPA®'s approval for the CV Indication, the VASCEPA® label was modified to remove the CV Limitation of Use and add the CV Indication, among other changes. *Compare* Ex. D, *with* Exs. E and F.

64. To illustrate, the Highlights of Prescribing Information of the VASCEPA® label as approved by FDA in December 2019 lacks the CV Limitation of Use:

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VASCEPA® safely and effectively. See full prescribing information for VASCEPA.

VASCEPA® (icosapent ethyl) capsules, for oral use
Initial U.S. Approval: 2012

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	12/2019
Warnings and Precautions, Atrial Fibrillation/Flutter (5.1)	12/2019
Warnings and Precautions, Bleeding (5.3)	12/2019

----------INDICATIONS AND USAGE----------

VASCEPA is an ethyl ester of eicosapentaenoic acid (EPA) indicated:

- as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and
  - established cardiovascular disease or
  - diabetes mellitus and 2 or more additional risk factors for cardiovascular disease. (1)
- as an adjunct to diet to reduce TG levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:

- The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

----------DOSAGE AND ADMINISTRATION----------

See Ex. D. This is in contrast with the 2019 LOVAZA® label which still contains the CV Limitation of Use. *See* Ex. S.

65. The current VASCEPA® label instructs, recommends, and encourages administering icosapent ethyl in combination with a statin to patients with baseline triglycerides ≥ 150 mg/dL to reduce the risk of a cardiovascular event in a daily dose of 4 grams per day. *See* Ex. D. Notably, FDA did not include an upper limit on the triglyceride range for the CV Indication.

66. FDA's December 13, 2019 approval of VASCEPA® for the CV Indication was hailed as "a major milestone in cardiovascular prevention." Ex. I. As the lead investigator for the REDUCE-IT study explained, "Nothing this significant has happened in the world of cardiovascular prevention since the introduction of statins nearly three decades ago. Many patients stand to benefit from this historic advance in care." *Id.*

67. On information and belief, following VASCEPA®'s approval for the CV Indication and the concurrent removal of the CV Limitation of Use from the VASCEPA® label, healthcare providers rapidly associated administration of icosapent ethyl together with a statin as a method for reducing risk of cardiovascular events in patients with baseline triglycerides ≥ 150 mg/dL.

68. On information and belief, the Hikma Defendants learned that FDA approved VASCEPA® for the CV Indication on or around December 13, 2019 because, on information and belief, the Hikma Defendants regularly monitor the approval status of brand-name drugs serving as the RLD for its generic drug candidates, and thus learned of VASCEPA® additional approval either from the FDA's press release announcing the same (Ex. J), Amarin's press release announcing the same (Ex. I), or in some other form.

69. On information and belief, Health Net, which is a health insurance provider, learned that FDA approved VASCEPA® for the CV Indication on or around December 13, 2019 because, on information and belief, Health Net regularly monitors the approved indications for drugs that it covers for its health insurance plans and on its formulary lists and for which it directs or provides payment.

D. Amarin Listed the Asserted Patents Patent in the FDA's Orange Book as Covering VASCEPA®

70. In conjunction with NDA No. 202057, Amarin submitted patent information relating to VASCEPA® to FDA for listing in the "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly referred to the "Orange Book," which provides notice concerning patents covering FDA-approved drugs.

71. On January 9, 2020, Amarin timely submitted patent information regarding the '537 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

72. The ’537 patent was listed in the Orange Book on or about January 10, 2020 with patent use code U-2707, “Use of VASCEPA as an adjunct to statin therapy to reduce the occurrence of a cardiovascular event in an adult patient with hypercholesterolemia.”

73. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the ’537 patent.

74. On January 6, 2020, Amarin timely submitted patent information regarding the ’077 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

75. The ’077 patent was listed in the Orange Book on or about January 6, 2020 with patent use code U-2693, “Use of VASCEPA to reduce triglycerides in a mixed dyslipidemia adult patient with elevated triglyceride (TG) levels (>= 150 mg/dL) and on statin therapy.”

76. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the ’077 patent.

77. On March 20, 2020, Amarin timely submitted patent information regarding the ’861 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

78. The ’861 patent was listed in the Orange Book on or about March 20, 2020 with patent use code U-2756, “Use of VASCEPA as an adjunct to statin therapy to reduce the risk of cardiovascular death in an adult patient with established cardiovascular disease.”

79. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the ’861 patent.

80. On information and belief, the Hikma Defendants learned that Amarin listed the ’537, ’077, and ’861 patents in the Orange Book as covering VASCEPA® at or around their time of

listing in the Orange Book because, on information and belief, the Hikma Defendants regularly monitor the Orange Book for updated patent listings made for brand-name drugs serving as the RLD for their generic drug candidates.

81. On information and belief, Health Net monitors FDA approval of generic versions of drugs that are listed on its formularies, on which VASCEPA® was and still is listed. Exs. CC, DD, and EE. As such, Health Net would have been aware of the FDA-approved indication for the Hikma Defendants' generic version of VASCEPA®.

82. The Hikma Defendants' generic version of VASCEPA® was FDA approved for only the Severe Hypertriglyceridemia Indication, and not for the CV Indication.

83. It is known in the field, and Health Net would have been aware, that when a generic product is approved for fewer than all the indications than its corresponding branded drug, it is often because there are patents that cover the indications for which the generic is not approved.

84. It is known in the field, and Health Net would have been aware, that any patents covering a branded drug, such as VASCEPA®, are listed in the Orange Book. Thus, on information and belief, once the Hikma Defendants' generic version of VASCEPA® was approved with only the Severe Hypertriglyceridemia Indication, Health Net knew, or should have known, that the CV Indication was covered by patents, including the patents-in-suit, listed in the Orange Book.

85. Alternatively, on information and belief, Health Net was aware that the '537, '077, and '861 patents are listed in the Orange Book as covering VASCEPA® on or around the date that Plaintiffs filed the original Complaint in this matter asserting that the Hikma Defendants' generic version of VASCEPA® infringed those patents.

86. On November 30, 2020, Amarin issued a press release about the filing of the original Complaint. Ex. FF. The press release states that "Hikma has induced the infringement of U.S. Patent Nos. 9,700,537 (Composition for preventing the occurrence of cardiovascular event in multiple risk patient), 8,642,077 (Stable pharmaceutical composition and methods of using same), and 10,568,861 (Methods of reducing the risk of a cardiovascular event in a subject at risk for cardiovascular disease) by making, selling, offering to sell and importing generic icosapent ethyl capsules in or into the United States." It further states that Amarin is seeking:

> a permanent injunction against Hikma's unlawful inducement of infringing uses of its generic product to reduce cardiovascular risk and monetary damages in an amount sufficient to compensate Amarin for such infringement. Amarin is considering its legal options against similarly situated parties acting in concert with Hikma by making or selling any drug product or component thereof covered by the subject patents, or inducing others to do the same.

87. On December 11, 2020, Amarin sent a letter to the payer community, including Envolve, the Pharmacy Benefit Manager ("PBM") that Health Net, on information and belief, uses to manage its pharmacy benefits, concerning the launch of the Hikma Defendants' generic version of VASCEPA®. Ex. GG. In the letter, sent via electronic mail to Mr. Mike Flynn at Envolve Pharmacy Solutions, Inc. ("Envolve"), who Amarin uses as its point of contact for Health Net, Amarin explained that the Hikma Defendants' generic version of VASCEPA® is not FDA-approved for the CV Indication:

> Furthermore, Hikma's generic icosapent ethyl product is indicated as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. Severe (≥500 mg/dL) hypertriglyceridemia represents <10% of the overall utilization of VASCEPA. It is important to note that, unlike the Hikma generic, VASCEPA is also indicated for cardiovascular (CV) risk reduction on top of statin therapy. The ***Hikma generic does not have an FDA-approved indication for CV risk reduction***.

Ex. GG (emphasis added).

88. In the letter, Amarin also informed the recipients that it had "sued Hikma for patent infringement for encouraging use of its generic product in the CV risk reduction indication. Amarin maintains patent exclusivity for CV risk reduction, and the Hikma generic should not be dispensed for this indication." Ex. GG.

89. Thus, Health Net was or should have been aware that actions that encourage the sale or use of Hikma's generic version of VASCEPA® for the CV Indication would induce infringement of the patents-in-suit.

90. Further, on November 16, 2020, even before filing this lawsuit against Hikma, Amarin held a clinical review meeting with Envolve, which, on information and belief, provides PBM services to Health Net. This meeting was attended by several people from Health Net's PBM Envolve, including Mr. Mike Flynn, who served as Amarin's contact for Health Net. At that meeting, Amarin discussed the clinical data to support VASCEPA®'s CV Indication, as well as detailed how the approved indications on the labels for VASCEPA® and Hikma's generic version of VASCEPA® differed.

91. In the alternative, Health Net is at least aware as of the service of this Amended Complaint that its actions encourage the sale or use of Hikma's generic version of VASCEPA® for the CV indication, and that those actions would induce infringement of the patents-in-suit.

ACTS GIVING RISE TO THIS ACTION FOR THE HIKMA DEFENDANTS' INFRINGEMENT OF THE PATENTS-IN-SUIT

92. The Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the "Hatch-Waxman Act," amended the Federal Food, Drug, and Cosmetic Act ("FDCA") and governs approvals of generic drugs. Under Section 505(j) of the amended FDCA, codified at 21 U.S.C. § 355(j), companies wishing to bring a generic version of a branded

prescription drug to market can submit an Abbreviated New Drug Application ("ANDA") to the FDA.

93. The ANDA process allows the generic drug company to avoid the expensive clinical trials required of an NDA holder to demonstrate a drug's safety and effectiveness by relying on the original NDA submission for that purpose. This process results in an enormous cost and time savings to the generic drug company. Reliance on the innovator company's data and the ability to "free ride" on the innovator company's development saves the generic drug company millions of dollars and years in development and clinical research costs.

94. The Hatch-Waxman Act also contains provisions meant to balance the competing interests of innovator and generic drug companies. When seeking ANDA approval, the generic applicant must consult the Orange Book and make certain certifications with respect to each patent listed for the branded drug. The generic applicant can certify that no patent information appears in the Orange Book ("Paragraph I certification"); that the listed patent has already expired ("Paragraph II certification"); that the applicant will not market the generic version before the date on which the patent will expire ("Paragraph III certification"); or that the patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA is submitted ("Paragraph IV certification"). 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV). When a Paragraph IV certification is made, the generic applicant must also provide notice of the certification to the innovator company, who can choose to enforce its patents in federal court.

95. When the listed patent is a method-of-use patent, like the Asserted Patents, the generic applicant can attempt to seek FDA approval to label its drug only for uses not covered by the patent, in which case a statement is submitted under 21 U.S.C. § 355(j)(2)(A)(viii), commonly known as a "Section viii statement" or "Section viii carve-out," in place of a patent certification.

The generic applicant is not obligated to provide notice of a Section viii statement to the innovator company.

96. For an Orange Book-listed method-of-use patent that has not expired, whether to make a Paragraph III or Paragraph IV certification or a Section viii statement is a calculated business decision the generic applicant makes after evaluating the associated commercial risks.

97. It is the generic applicant's responsibility to ensure that the marketing and sale of its ANDA product (including the associated labeling, not limited to the Indications and Usage section) pursuant to a Section viii statement does not infringe the patents referenced in the Section viii statement. Indeed, FDA describes its role with respect to patents as "ministerial," has observed that it "lack[s] expertise in patent matters," and does not make patent infringement determinations when reviewing the labeling associated with a Section viii statement. 68 Fed. Reg. 36,683. Courts have found generic manufacturer's labels, approved subject to a Section viii statement, to nonetheless be evidence of patent infringement.

98. The Orange Book also contains therapeutic equivalence ratings for multisource prescription drug products. The agency developed these ratings in the 1970s in response to states that requested guidance as they implemented laws to encourage generic substitution. FDA has explained that an AB rating reflects a decision that a generic drug is therapeutically equivalent to a branded drug when the generic drug is used as labeled, and it does not reflect a decision of therapeutic equivalence for off-label uses.

99. On information and belief, on or about September 21, 2016, Hikma (through its predecessor) submitted ANDA No. 209457 for generic copies of VASCEPA® (icosapent ethyl) 1 mg under section 505(j) of the FDCA.

100. On information and belief, Hikma Pharmaceuticals USA, Inc. is the current owner of ANDA No. 209457.

101. As an ANDA filer, Hikma was required to provide to FDA patent certifications or Section viii statements addressing each of the patents timely listed in the Orange Book for VASCEPA® before FDA finally approved ANDA No. 209457. 21 C.F.R. § 314.94(a)(12).

102. At the time the Asserted Patents were listed in the Orange Book, FDA had not yet finally approved ANDA No. 209457. Thus, before FDA's final approval of ANDA No. 209457 in May 2020, Hikma was required to provide to FDA either patent certifications or Section viii statements as to the Asserted Patents. 21 C.F.R. § 314.94(a)(12).

103. On information and belief, Hikma knew, at least because of the Asserted Patents' listing in the Orange Book as covering VASCEPA®, that use of icosapent ethyl just like VASCEPA® would constitute direct infringement of the Asserted Patents.

104. On information and belief, Hikma submitted to FDA Section viii statements with respect to the Asserted Patents after January 9, 2020 and before May 21, 2020.

105. On information and belief, on or about May 21, 2020, the FDA granted final approval for Hikma's ANDA No. 209457 with Section viii statements for the Asserted Patents, including labeling prepared by Hikma with full knowledge of the Asserted Patents.

106. On information and belief, a true and correct copy of Hikma's labeling that is provided with its icosapent ethyl capsules, and reflecting its Section viii statement strategy for the Asserted Patents, is attached hereto as Exhibit K ("Hikma's Label").

107. Like the current VASCEPA® label, Hikma's Label does not include the CV Limitation of Use. *Compare* Ex. D *with* Ex. K at Highlights of Prescribing Information and

Sections 1 and 14. As shown below, the relevant sections of Hikma's Label lack the CV Limitation of Use:

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ICOSAPENT ETHYL CAPSULES safely and effectively. See full prescribing information for ICOSAPENT ETHYL CAPSULES.

ICOSAPENT ETHYL capsules, for oral use
Initial U.S. Approval: 2012

RECENT MAJOR CHANGES

Warnings and Precautions, Atrial Fibrillation/Flutter (5.1)	12/2019
Warnings and Precautions, Bleeding (5.3)	12/2019

INDICATIONS AND USAGE

Icosapent ethyl capsules are an ethyl ester of eicosapentaenoic acid (EPA) indicated:

- as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:

- The effect of icosapent ethyl on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

DOSAGE AND ADMINISTRATION

Ex. K at Highlights of Prescribing Information.

1 INDICATIONS AND USAGE

Icosapent ethyl is indicated:

- as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Limitations of Use

The effect of icosapent ethyl on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

Ex. K at § 1.

Icosapent ethyl 4 grams per day reduced median TG, VLDL-C, and Apo B levels from baseline relative to placebo. The reduction in TG observed with icosapent ethyl was not associated with elevations in LDL-C levels relative to placebo.

Ex. K at § 14.

108. On information and belief, from the time Hikma submitted ANDA No. 209457 to FDA in September 2016 and until Hikma submitted to FDA Section viii statements with respect

to the Asserted Patents, the proposed label for Hikma's icosapent ethyl capsules prepared by Hikma contained the CV Limitation of Use. On information and belief, on or about the date on which it submitted to FDA Section viii statements with respect to the Asserted Patents, Hikma intentionally amended the proposed labeling for its icosapent ethyl capsules to remove the CV Limitation of Use. On information and belief, with knowledge of the Asserted Patents, Hikma removed the CV Limitation of Use from the Hikma Label so that healthcare providers and patients would believe that Hikma's generic icosapent ethyl capsules could be and should be used just like VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®. Hikma's removal of the CV Limitation of Use from the Hikma Label demonstrates Hikma's specific intent to induce infringement of the Asserted Patents.

109. On information and belief, Hikma has always intended for its icosapent ethyl capsules to be used in the place of VASCEPA® for all of VASCEPA®'s uses. On information and belief, Hikma developed its product based on market assumptions that included the entirety of VASCEPA®'s sales, not just for sales resulting from treatment pursuant to the Severe Hypertriglyceridemia Indication.

110. On information and belief, Hikma was and is aware that over 75% of the sales of VASCEPA® since 2013 are for uses other than the Severe Hypertriglyceridemia Indication, including uses to reduce CV events. Ex. W (Nevada Case, D.I. 373) ¶ 115. At the trial concerning Hikma's infringement of the patents related to the Severe Hypertriglyceridemia Indication,[1] Hikma, through its counsel, repeatedly argued that the "vast majority" of prescriptions for VASCEPA® are for uses other than for the Severe Hypertriglyceridemia Indication. Ex. W

[1] Amarin Pharma, Inc. et al. v. Hikma Pharmaceuticals USA, Inc. et al., Case No. 1:16-cv-02525-MMD-NJK (D. Nev.) [hereinafter the "Nevada Case"].

(Nevada Case, D.I. 377) ¶ 440; Ex. AA (Nevada Case Trial Tr.) at 1252-1253 (Hoffman); *see also* Ex. Q (Nevada Case DDX 1-36); Ex. R (Nevada Case DDX 8.13). At trial in the Nevada Case, Hikma, through its counsel, acknowledged that there are "several reasons why a physician might prescribe Vascepa (or the Hikma Defendants' ANDA Products) … other than to treat severe hypertriglyceridemia," including to reduce cardiovascular risk. Ex. W (Nevada Case, D.I. 377) ¶ 116.

111. On information and belief, Hikma is aware and intends that its generic product, which Hikma describes as AB rated to VASCEPA® for "hypertriglyceridemia," will be substituted for all VASCEPA® prescriptions, not just the prescriptions directed to the Severe Hypertriglyceridemia Indication. *See* Ex. T ("Hikma's Website"). Hikma Pharmaceuticals PLC issued a press release on March 31, 2020 referencing "Hikma's generic version of Amarin Corporation's Vascepa® (icosapent ethyl) 1 gm capsules." A true and correct copy of this press release, obtained from Hikma's website is attached hereto as Exhibit L ("Hikma's March 2020 Press Release").

112. In Hikma's March 2020 Press Release, Hikma stated that "Vascepa® is a prescription medicine that is indicated, *in part*, as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. According to IQVIA, US sales of Vascepa® were approximately $919 million in the 12 months ending February 2020." Ex. L (emphasis added).

113. The $919 million in Vascepa® sales referenced in Hikma's March 2020 Press Release includes sales for ***all uses*** of Vascepa®, including the CV Indication (which Hikma knew made up more than 75% of VASCEPA®'s sales).

114. Hikma's March 2020 Press Release does not state that Hikma's "generic version" of VASCEPA® should not be used for the CV Indication or that the effect of icosapent ethyl on cardiovascular mortality and morbidity had not been determined. *See* Ex. L.

115. Hikma's March 2020 Press Release communicates to and instructs healthcare providers and patients that Hikma's "generic version" of VASCEPA® ***should be used for all the same indications*** as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®, and thus promotes and encourages that use.

116. Hikma's March 2020 Press Release demonstrates Hikma's specific intent to encourage infringement of the Asserted Patents.

117. On information and belief, in mid-October 2020, Hikma purported to remove the March 2020 Press Release from the "Newsroom" page of its website. On information and belief, that action demonstrates Hikma's knowledge that the March 2020 Press Release encourages healthcare providers and patients to use Hikma's "generic version" of VASCEPA® for all the same indications as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA® and as claimed in the Asserted Patents. However, Hikma's March 2020 Press Release is still accessible as of November 30, 2020 on Hikma's website at the following URL: https://www.hikma.com/media/2766/vascepa-press-release-positive-march-30-2020-720pmet-final.pdf.

118. Hikma Pharmaceuticals PLC issued a press release on September 3, 2020 referencing "Hikma's generic version of Vascepa® (icosapent ethyl) 1 gm [capsules]." A true and correct copy of this press release is attached hereto as Exhibit M ("Hikma's September 2020 Press Release").

119. In Hikma's September 2020 Press Release, Hikma stated that "Vascepa® is a prescription medicine that is indicated, *in part*, as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. According to IQVIA, US sales of Vascepa® were approximately $1.1 billion in the 12 months ending July 2020." Ex. M (emphasis added).

120. The $1.1 billion in Vascepa® sales referenced in Hikma's September 2020 Press Release includes sales for all uses of Vascepa®, including the CV Indication (which Hikma knew made up more than 75% of sales).

121. Hikma's September 2020 Press Release does not state that Hikma's "generic version" of VASCEPA® should not be used for the CV Indication or that the effect of icosapent ethyl on cardiovascular mortality and morbidity had not been determined. *See* Ex. M.

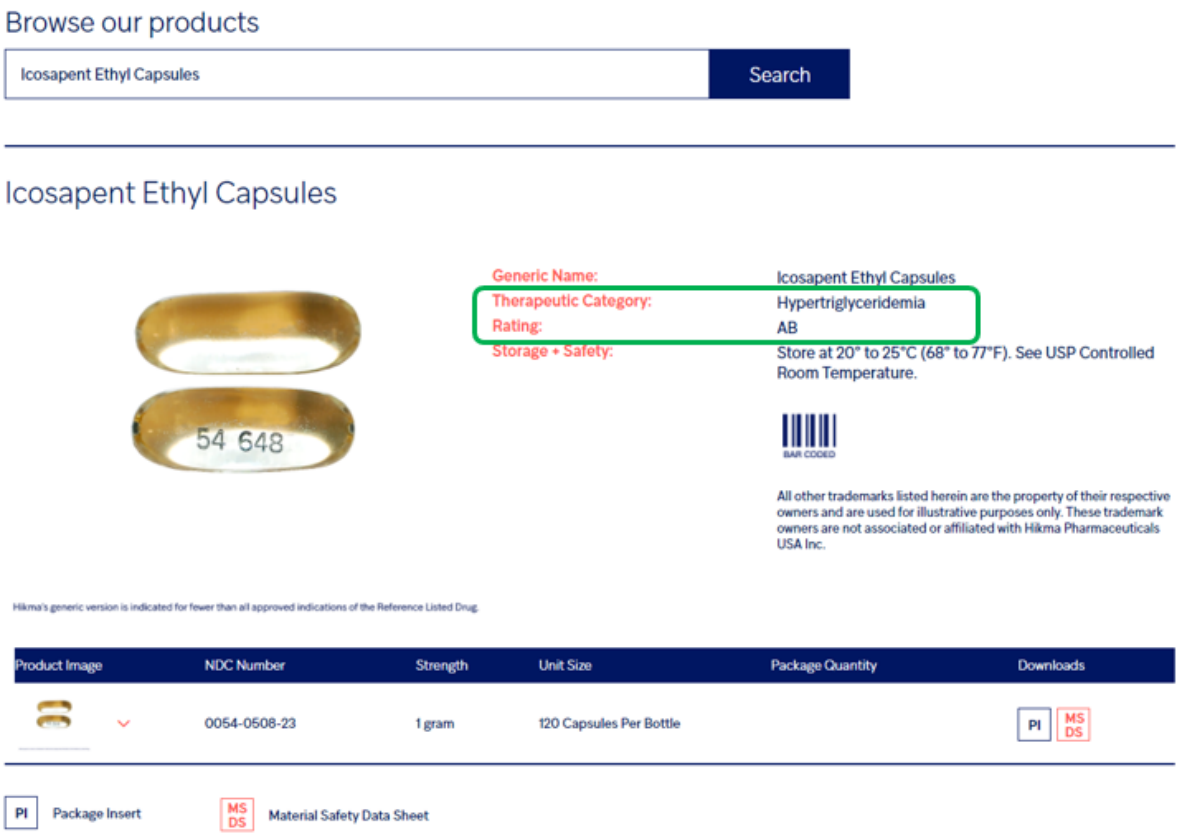
122. Hikma's September 2020 Press Release communicates to and instructs healthcare providers and patients that Hikma's "generic version" of VASCEPA® ***should be used for all the same indications*** as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA® and as claimed in the Asserted Patents, and thus promotes and encourages that use.

123. Hikma's September 2020 Press Release demonstrates Hikma's specific intent to encourage infringement of the Asserted Patents.

124. On information and belief, in mid-October 2020, Hikma purported to remove the September 2020 Press Release from the "Newsroom" page of its website. On information and belief, that action demonstrates Hikma's knowledge that the September 2020 Press Release encourages healthcare providers and patients to use Hikma's "generic version" of VASCEPA® for all the same indications as VASCEPA®, including to reduce the risk of CV events per the CV

Indication awarded to VASCEPA®. However, Hikma's September 2020 Press Release is still accessible as of November 30, 2020 on Hikma's website at the following URL: https://www.hikma.com/media/2836/vascepa-statement-september-2020-vfinal.pdf.

125. Further, Hikma has launched its generic version of VASCEPA® and promoted to the market, including on its website, that it is "AB" rated in the "Therapeutic Category: Hypertriglyceridemia." A copy of the product information for Hikma's Icosapent Ethyl Capsules communicated on Hikma's Website is reproduced below with a green annotation.



See Ex. T.

126. Notably, the "Therapeutic Category" information for Hikma's Icosapent Ethyl Capsules communicated on Hikma's Website—"Hypertriglyceridemia"—does not match and is broader than the Indications and Usage sections of Hikma's Label, which includes only the Severe

Hypertriglyceridemia Indication (i.e., triglycerides ≥ 500 mg/dL). Moreover, Hikma's Label does not include the CV Limitation of Use included on the original VASCEPA® label. *Compare* Ex. K, *with* Ex. E.

127. Hikma's March and September 2020 Press Releases, together with Hikma's Website that identifies and describes its generic version of VASCEPA® as "AB" rated in the therapeutic category "Hypertriglyceridemia," and the Hikma Label, instruct, promote, and encourage healthcare providers and patients to administer Hikma's generic icosapent ethyl capsules to hypercholesterolemia patients with triglycerides of at least about 150 mg/dL and HDL-C of less than about 40 mg/dL and who are taking a statin, to reduce the risk of occurrence of a cardiovascular event, as covered by claims of the Asserted Patent.

128. As described above, the totality of Hikma's March 2020 Press Release and September 2020 Press Release, the Hikma Label, and the Hikma Website, instruct, promote, and encourage healthcare providers and patients to administer Hikma's icosapent ethyl capsules just like VASCEPA® including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®.

129. On information and belief, Hikma knew that when an AB-rated generic drug is available, many pharmacies and/or third party payers of prescription drugs (e.g., health insurance plans, Medicare and Medicaid programs) have adopted policies that encourage or require the substitution of the AB-rated generic drugs for the branded drugs, regardless of whether the generic drug label includes all the indications in the branded drug labeling. Some (but not all) states have similar policies. As a result, on information and belief, Hikma knew and intended that its generic product would be substituted for all VASCEPA® prescriptions, not just the prescriptions directed to the Severe Hypertriglyceridemia Indication.

130. Like the VASCEPA® label, Hikma's Label encourages, promotes, and instructs treating patients who present with, as determined by blood draw (*see, e.g.*, Ex. K, § 2 ("Assess lipid levels before initiating therapy.")), **(a)** a baseline total cholesterol level of ≥ 220 mg/dL, which a skilled artisan would recognize as signifying hypercholesterolemia (*see, e.g.*, *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "TG (mg/dL)" is 254)); **(b)** a baseline triglyceride level ≥ 150 mg/dL (*see, e.g.*, *id.* (for treatment group, "baseline" "TG (mg/dL)" is 680); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized . . . trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]. . . .")); **(c)** a baseline HDL-C level less than 40 mg/dL (*see, e.g.*, *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "HDL-C (mg/dL)" is 27)); and who are **(d)** concomitantly receiving statin therapy, including for example 10-80 mg of atorvastatin (*see, e.g.*, *id.* § 14.2 ("Twenty-five percent of patients were on concomitant statin therapy"); *id.* § 12.3 ("Atorvastatin: In a drug-drug interaction study of 26 healthy adult subjects, icosapent ethyl 4 g/day at steady-state did not significantly change the steady-state AUC_{τ} or C_{max} of atorvastatin, 2-hydroxyatorvastatin, or 4-hydroxyatorvastatin when co-administered with atorvastatin 80 mg/day at steady state.")), and **(e)** have not had a previous cardiovascular event (*see, e.g.*, *id.* at Patient Information leaflet ("Heart rhythm problems which can be serious and cause hospitalization have happened *in people who take icosapent ethyl, especially in people who have* heart (cardiovascular) disease or *diabetes with a risk factor for heart (cardiovascular) disease*, or who have had heart rhythm problems in the past.") (emphases added); *id.* § 17 ("Advise the patient to read the FDA-approved patient labeling before starting icosapent ethyl (Patient Information).")).

131. Like the VASCEPA® label, Hikma's Label encourages, promotes, and instructs treating patients who present with **(a)** established cardiovascular disease (*see, e.g.*, Ex. K at Patient

Information leaflet ("Heart rhythm problems which can be serious and cause hospitalization have happened *in people who take icosapent ethyl, especially in people who have heart (cardiovascular) disease* or diabetes with a risk factor for heart (cardiovascular) disease, or who have had heart rhythm problems in the past.") (emphasis added); *id.* § 17 ("Advise the patient to read the FDA-approved patient labeling before starting icosapent ethyl (Patient Information)."), **(b)** a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL (*see, e.g.*, *id.* § 14.2 ("Patients whose baseline TG levels were between 500 and 2,000 mg/dL were enrolled in this study . . . ."); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized . . . trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]. . . .")), and **(c)** a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL (*see, e.g.*, *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "LDL-C (mg/dL)" is 91)), **(d)** with about 4 g of icosapent ethyl (ethyl icosapentate) per day (*see id.* § 2.2)).

132. In addition, Hikma's 2020 Label states in its Patient Information leaflet: "Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." *See* Ex. K. At trial, one of Hikma's physician experts pointed to this sentence during trial that "most often we use this medication for reasons other than the MARINE data, and in the patient information section it specifically tells the patients that we would potentially do that." Ex. X (Nevada Case, Trial Tr.) at 617.

133. Thus, a healthcare provider with knowledge of the significance of FDA approving VASCEPA® for the CV Indication, and the consequential removal of the CV Limitation of Use from the VASCEPA® label in conjunction with that approval, the contents of Hikma's March and September 2020 Press Releases, Hikma's Website, and Hikma's Label, will inevitably practice at least the methods the '537 and '861 patents by administering icosapent ethyl to at least some

patients with the characteristics required by those claims and at a dose of 4g per day, including for a period effective to reduce risk of cardiovascular death.

134. Like the VASCEPA® label, Hikma's Label encourages, promotes and instructs treating patients who present with **(a)** mixed dyslipidemia (*see, e.g.*, Ex. K, § 14.2 ("Patients whose baseline TG levels were between 500 and 2,000 mg/dL were enrolled in this study . . . ."); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized . . . trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]. . . ."); *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "LDL-C (mg/dL)" is 91)); *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "HDL-C (mg/dL)" is 27), and **(b)** who are on statin therapy (*see, e.g.*, *id.* § 14.2 ("Twenty-five percent of patients were on concomitant statin therapy"), with **(c)** a pharmaceutical composition comprising about 4 g of icosapent ethyl (ethyl eicosapentaenoate) per day and not more than about 5%, by weight of all fatty acids, docosahexaenoic acid or its esters (*see, e.g.*, *id.* § 2.2; Nevada Case, D.I. 381 (Bench Order) at 8 ("The 'pharmaceutical composition' in Hikma's ANDA Product, if approved, will comprise 'at least about 96% by weight of all fatty acids present, ethyl eicosapentaenoate[,] and substantially no docosahexaenoic acid or its esters . . . ."), to **(d)** effect a reduction in fasting triglyceride levels in the subject (*see, e.g.*, Ex. K at § 1 ("Icosapent ethyl is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.")); and **(e)** wherein the patients exhibit a reduction in hs-CRP compared to placebo control (*see, e.g.*, Ex. U (Ballantyne) at abstract, Fig. 3, 5.).

135. For all the reasons set forth above, Hikma knows of and specifically intends for healthcare providers to administer its icosapent ethyl capsules in the place of VASCEPA® and to practice the methods of the Asserted Patents by administering icosapent ethyl to at least some patients with the characteristics required by those claims in the dose and for the duration required

by those claims, and for the purposes recited in those claims, and its labeling and marketing materials promote, encourage, and instruct healthcare providers to practice the methods of the Asserted Patents.

ACTS GIVING RISE TO THIS ACTION FOR HEALTH NET'S INFRINGEMENT OF THE PATENTS-IN-SUIT

136. Amarin incorporates paragraphs 1 to 135 as if fully set forth herein.

137. On information and belief, Health Net offers a variety of different health insurance plans and /or prescription drug benefit plans, on its own or through its subsidiaries, throughout the United States. On information and belief, Health Net contracts with Envolve to provide pharmacy benefit management ("PBM") services for many of Health Net's plans. On information and belief, Health Net sets the benefits and chooses which drugs it will cover and pay for on its formularies.

138. Before the launch of the Hikma Defendants' generic version of VASCEPA®, VASCEPA® was the only pure EPA product approved by FDA.

139. VASCEPA® was covered by Health Net health insurance plans and appeared on formularies used by Health Net as a covered drug before the approval and launch of the Hikma Defendants' generic version of VASCEPA®. At that time, it was the only pure EPA (icosapent ethyl) product covered by or on formularies used by Health Net.

140. After the launch of the Hikma Defendants' generic version of VASCEPA®, Health Net added the generic product to formularies, meaning that it would provide insurance coverage and/or payment for Hikma's generic version of VASCEPA®.

141. For example, the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary, which, on information and belief, are both formularies for Health Net's Medicare business, include Hikma's generic version of VASCEPA®, referred to as "icosapent ethyl caps."

Exs. CC and DD. In addition, Hikma's generic version of VASCEPA® is included in Health Net's 2021 Essential Rx Drug List formulary. Ex. EE.

142. Indeed, the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary encourage the prescription and use of Hikma's generic version of VASCEPA®.

143. VASCEPA® is on these formularies as a tier 3 drug. Ex. CC at 25; Ex. DD at 23. By contrast, Hikma's generic version of VASCEPA®, referred to as "icosapent ethyl caps" (in lower case italics), is on the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary as a tier 1 drug. *Id.*

144. Health Net makes no distinction on its formulary listing for Hikma's generic version of VASCEPA® with respect to the CV Indication versus the Severe Hypertriglyceridemia Indication, even though Hikma's generic version of VASCEPA® is not approved for the former. Thus, Hikma's generic version of VASCEPA® is on tier 1 for all potential uses of the drug, and not merely for its approved Severe Hypertriglyceridemia Indication. By so doing, Health Net has intentionally disregarded the patent rights associated with the CV Indication asserted in this action.

145. On information and belief, the placement of a drug on a lower tier leads to a lower patient copayment than placement of a drug on a higher tier. Thus, on information and belief, as a tier 1 drug, Hikma's generic version of VASCEPA® has a lower patient copayment than VASCEPA®.

146. Health Net's inclusion of the Hikma Defendants' generic version of VASCEPA® at tier 1 on the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary encourages pharmacists to dispense it and patients to use it instead of VASCEPA® given VASCEPA®'s placement on tier 3, for both the Severe Hypertriglyceridemia Indication and the

patented CV Indication, even though Hikma's generic version of VASCEPA® is not approved by the FDA for the patented CV Indication.

147. The Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary also promote and encourage the use of Hikma's generic version of VASCEPA® in other ways. Both formularies state that "[o]ur plan covers both brand name and generic drugs. A generic drug is approved by FDA as having the same active ingredient as the brand name drug. Generally, generic drugs cost less than brand name drugs." Exs. CC and DD at iii.

148. Both formularies also state that "We may immediately remove a brand name drug on our Drug List if we are replacing it with a new generic drug that will appear on the same or lower cost sharing tier and with the same or fewer restrictions. ***Also, when adding the new generic drug, we may decide to keep the brand name drug on our Drug List, but immediately move it to a different cost-sharing tier or add new restrictions***. If you are currently taking that brand name drug, we may not tell you in advance before we make that change, but we will later provide you with information about the specific change(s) we have made." Exs. CC and DD at i.

149. In addition, on information and belief, with the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary, Health Net covers and directs payment for Hikma's generic version of VASCEPA® for both the Severe Hypertriglyceridemia Indication, for which it is FDA approved, and the CV Indication, for which Hikma did not seek or receive FDA approval.

150. Because Health Net covers and directs payment for the Hikma Defendants' generic version of VASCEPA® for prescriptions for both the Severe Hypertriglyceridemia Indication and the CV Indication, Health Net knows and intends that it is covering and directing payment for prescriptions of Hikma's generic version of VASCEPA® for the CV Indication.

151. On information and belief, Health Net knows that when an AB-rated generic drug is available, many pharmacies have adopted policies that encourage or require the substitution of the AB-rated generic drugs for the branded drugs, regardless of whether the generic drug label includes all the indications in the branded drug labeling. Some (but not all) states have similar policies. As a result, on information and belief, Health Net knew and intended that its generic product would be substituted for all VASCEPA® prescriptions, not just the prescriptions directed to the Severe Hypertriglyceridemia Indication.

152. Indeed, available market data indicates that less than 10% of the prescriptions of VASCEPA® are currently in the Severe Hypertriglyceridemia population and thus could be covered under the Severe Hypertriglyceridemia Indication. And Amarin stated in its December 11, 2020 letter to payers that "[s]evere (≥500 mg/dL) hypertriglyceridemia represents <10% of the overall utilization of VASCEPA." Ex. GG. On information and belief, Health Net would have been aware of this or similar data and would have known and understood that the vast majority of prescriptions for VASCEPA® are for the CV Indication, for which Hikma's generic version of VASCEPA® does not have FDA approval. Thus, Health Net would have known, understood, and intended that, in covering and directing payment for Hikma's generic version of VASCEPA® for any indication it may be prescribed for, it was covering and directing payment for Hikma's generic version of VASCEPA® for the CV Indication.

153. In addition, before the approval of Hikma's generic version of VASCEPA®, VASCEPA® was on Health Net's Essential Rx Drug List, which, on information and belief, relates to Health Net's commercial business, as a covered drug, but it was only covered if it was being prescribed for a condition that was listed on Health Net's Prior Authorization ("PA") form for VASCEPA®. Ex. HH.

154. Health Net's PA for VASCEPA® lists both of the FDA-approved indications for VASCEPA®—the Severe Hypertriglyceridemia Indication and the CV Indication. Ex. HH. It then details the criteria that must be met before VASCEPA® can be covered. For "Initial Approval Criteria," the PA includes two options: (1) "Hypertriglyceridemia without ASCVD," where the patient has "[f]asting triglycerides ≥ 500 mg/dL," and (2) "Reduction of Cardiovascular Disease Risk" with "[d]ocumentation (labs must be within 90 days) of fasting triglycerides between 150-499 mg/dL" and, "[f]or members on statin therapy," "Vascepa is prescribed in conjunction with a statin at the maximally tolerated dose." Ex. HH.

155. The VASCEPA® PA, and the information that it requires be collected, demonstrates that Health Net is aware that VASCEPA® is prescribed for two indications—the Severe Hypertriglyceridemia Indication and the CV Indication.

156. After the launch of the Hikma Defendants' generic version of VASCEPA®, Health Net added that generic version to its Health Net Essential Drug list. (Ex EE (formulary from website) at 37.) Health Net characterizes this list as including "a list of drugs covered by Health Net" that "is selected by Health Net, along with a team of health care providers." Ex. II.

157. The Health Net Essential Rx Drug List currently includes Hikma's generic version of VASCEPA®, referred to as "icoaspent ethyl caps." Ex. EE at 28. As with the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary, the Health Net Essential Rx Drug list includes VASCEPA® as a tier 3 drug and Hikma's generic version of VASCEPA® (icosapent ethyl caps) as a tier 1 drug. (*Id.*)

158. When an insurance provider covers a medication, and particularly when it covers it at a lower tier, it employs the economic incentive of lower patient copayments to encourage pharmacists to fill prescriptions with that medication, and encourages patients to use that

medication. Health Net's coverage of the Hikma Defendants' generic version of VASCEPA® as a tier 1 drug on the Essential Rx Drug List encourages pharmacists to dispense it and patients to use it, particularly as compared to VASCEPA®, which is on tier 3.

159. In addition, like it does for VASCEPA®, the Health Net Essential Rx Drug List requires a PA for the Hikma Defendants' generic version of VASCEPA® that details the criteria that must be met before it can be covered. Ex. EE at 28. On information and belief, the PA used for the Hikma Defendants' generic version of VASCEPA® collects the same information as the PA for VASCEPA®. Thus, it collects information as to whether the drug is being prescribed for the Severe Hypertriglyceridemia Indication or the CV Indication. Health Net's use of this PA for the Hikma Defendants' generic version of VASCEPA® demonstrates that Health Net knows what indication the product is being prescribed for, and chooses to cover it for both indications.

160. On information and belief, Health Net, for the Health Net Essential Rx Drug List, covers the Hikma Defendants' generic version of VASCEPA® if it meets any of the conditions on the PA. In other words, on information and belief, Health Net covers the Hikma Defendants' generic version of VASCEPA® for prescriptions for both the Severe Hypertriglyceridemia Indication and the CV Indication. And based on the PA, Health Net knows and intends that it is covering prescriptions of Hikma's generic version of VASCEPA® for the CV Indication.

161. Because Health Net, on its the Health Net Essential Rx Drug List, covers and directs payment for the Hikma Defendants' generic version of VASCEPA®, for prescriptions for patients meeting either the Severe Hypertriglyceridemia Indication or the CV Indication, it is aware and intends and causes some pharmacies to dispense, and some patients to use, the product for the CV Indication.

162. On information and belief, based on Health Net's actions, pharmacies are dispensing, and patients are using, Hikma's generic version of VASCEPA® for the CV indication. Indeed, current data shows that Hikma's generic version of VASCEPA® has over 20% of the total volume of VASCEPA® for Health Net's business.

COUNT I

(Infringement of the '537 Patent Under 35 U.S.C. § 271(b) by the Hikma Defendants)

163. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

164. On information and belief the Hikma Defendants have been and are inducing others to infringe the '537 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise promoting and distributing highly pure icosapent ethyl capsules to reduce the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin.

165. On information and belief, healthcare providers administering and/or patients using the Hikma Defendants' generic version of Vascepa® capsules within the United States do so in combination with a statin to, among other reasons, reduce the occurrence of a cardiovascular event in the patient population recited in claim 1 of the '537 patent, and thus directly infringe at least one claim of the '537 patent.

166. On information and belief, the Hikma Defendants possessed the specific intent to encourage direct infringement of the '537 patent. On information and belief, the Hikma

Defendants knew about the ’537 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 121.

167. Alternatively, the Hikma Defendants subjectively believed that there was a high probability that the use of icosapent ethyl capsules for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin, was protected by a valid patent, and that the activities referenced in paragraph 121 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

168. On information and belief, the Hikma Defendants knew that the administration or use of their generic version of VASCEPA® would be for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin, and so would be an act of direct infringement of the ’537 patent, and that the activities referenced in paragraph 121 would actively induce direct infringement of the ’537 patent. On information and belief, despite such knowledge, the Hikma Defendants have been and are actively inducing the infringement of the ’537 patent by others, and are doing do willfully and deliberately.

169. On information and belief, the Hikma Defendants will continue to induce infringement of the ’537 patent unless and until enjoined by the Court.

170. As a result of the Hikma Defendants’ inducement of infringement of the ’537 patent, Plaintiffs have suffered damages, including lost profits.

COUNT II

(Infringement of the ’077 Patent Under 35 U.S.C. § 271(b) by the Hikma Defendants)

171. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

172. On information and belief the Hikma Defendants have been and are inducing others to infringe the ’077 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise promoting and distributing highly pure icosapent ethyl capsules to reduce triglycerides in a subject with mixed dyslipidemia by administering about 4 g of ethyl eicosapentaenoate per day.

173. On information and belief, healthcare providers administering and/or patients using 4 g per day of the Hikma Defendants’ generic version of Vascepa® capsules within the United States do so, among other reasons, to reduce fasting triglyceride and hs-CRP levels in patients with mixed dyslipidemia, and thus directly infringe at least claim 8 of the ’077 patent.

174. On information and belief, the Hikma Defendants possessed the specific intent to encourage direct infringement of the ’077 patent. On information and belief, the Hikma Defendants knew about the ’077 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 129.

175. Alternatively, the Hikma Defendants subjectively believed that there was a high probability that the administration and use of 4 g per day of highly pure icosapent ethyl capsules for reducing fasting triglyceride and hs-CRP levels in subjects with mixed dyslipidemia was

protected by a valid patent, and that the activities referenced in paragraph 129 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

176. On information and belief, the Hikma Defendants knew that the administration or use of their generic version of VASCEPA® would be for daily administration of a 4 g/day dose to reduce fasting triglyceride and hs-CRP levels in subjects with mixed dyslipidemia, and so would be an act of direct infringement of the '077 patent, and that the activities referenced in paragraph 129 would actively induce direct infringement of the '077 patent. On information and belief, despite such knowledge, the Hikma Defendants have been and are actively inducing the infringement of the '077 patent by others, and are doing do willfully and deliberately.

177. On information and belief, the Hikma Defendants will continue to induce infringement of the '077 patent unless and until enjoined by the Court.

178. As a result of the Hikma Defendants' inducement of infringement of the '077 patent, Plaintiffs have suffered damages, including lost profits.

COUNT III

(Infringement of the '861 Patent Under 35 U.S.C. § 271(b) by the Hikma Defendants)

179. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

180. On information and belief the Hikma Defendants have been and are inducing others to infringe the '861 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise promoting and distributing highly pure icosapent ethyl capsules to reduce the risk of a cardiovascular death in a subject with established cardiovascular disease, including subjects with a fasting baseline triglyceride level of about 135 mg/dL to about

500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL, by administering about 4 g of ethyl icosapentate per day for a period effective to reduce risk of cardiovascular death.

181. On information and belief, healthcare providers administering and/or patients using 4 g per day of the Hikma Defendants' generic version of Vascepa® capsules within the United States do so, among other reasons, to reduce the risk of cardiovascular death in patients with established cardiovascular disease, including the patient population recited in claims 1 and 2, and thus directly infringe at least claim 1 and 2 of the '861 patent.

182. On information and belief, the Hikma Defendants possessed the specific intent to encourage direct infringement of the '861 patent. On information and belief, the Hikma Defendants knew about the '861 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 137.

183. Alternatively, the Hikma Defendants subjectively believed that there was a high probability that the administration and use of 4 g per day of icosapent ethyl capsules for reducing risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL, for a period effective to reduce risk of cardiovascular death, was protected by a valid patent, and that the activities referenced in paragraph 137 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

184. On information and belief, the Hikma Defendants knew that the administration or use of their generic version of VASCEPA® would be for daily administration of a 4 g/day dose to

reduce risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL, for a period effective to reduce risk of cardiovascular death, and so would be an act of direct infringement of the ’861 patent, and that the activities referenced in paragraph 137 would actively induce direct infringement of the ’861 patent. On information and belief, despite such knowledge, the Hikma Defendants have been and are actively inducing the infringement of the ’861 patent by others, and are doing do willfully and deliberately.

185. On information and belief, the Hikma Defendants will continue to induce infringement of the ’861 patent unless and until enjoined by the Court.

186. As a result of the Hikma Defendants’ inducement of infringement of the ’861 patent, Plaintiffs have suffered damages, including lost profits.

COUNT IV

(Infringement of the ’537 Patent Under 35 U.S.C. § 271(b) by Health Net)

187. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

188. On information and belief, by covering and/or directing or providing payment for others’ use of the Hikma Defendants’ generic version of VASCEPA® for the CV Indication, Health Net has been and is inducing others to use, offer to sell, sell, or otherwise promote or distribute the Hikma Defendants’ generic version of VASCEPA® to reduce the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering

the Hikma Defendants' generic version of VASCEPA® in combination with the statin, thereby infringing the '537 patent.

189. On information and belief, healthcare providers administering and/or patients using the Hikma Defendants' generic version of VASECPA® capsules within the United States do so in combination with a statin to, among other reasons, reduce the occurrence of a cardiovascular event in the patient population recited in claim 1 of the '537 patent, and thus directly infringe at least one claim of the '537 patent.

190. On information and belief, Health Net possessed the specific intent to encourage direct infringement of the '537 patent. On information and belief, Health Net knew about the '537 patent at least as of when the Hikma Defendants' generic version of VASCEPA® was launched with a label listing only the Severe Hypertriglyceridemia Indication; and/or when Amarin announced the filing of this lawsuit against the Hikma Defendants; and/or when Amarin sent a letter to payers, including Health Net's contracted Pharmacy Benefit Manufacturer Envolve, informing them of the filing of the patent exclusivity for the CV Indication and about this lawsuit against the Hikma Defendants, and before performing the activities referenced in paragraph 188. In the alternative, Health Net knows about the '537 patent at least as of the filing of this Amended Complaint and continues the activities referenced in paragraph 188.

191. Alternatively, Health Net subjectively believed that there was a high probability that the use of the Hikma Defendants' generic version of VASCEPA® for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by

administering highly pure EPA in combination with the statin, was protected by a valid patent, and that the activities referenced in paragraph 188 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded itself to the infringing nature of the use and sale of the Hikma Defendants' generic version of VASCEPA®.

192. On information and belief, Health Net knew that the administration or use of the Hikma Defendants' generic version of VASCEPA® would include the use for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin, and so would be an act of direct infringement of the '537 patent, and that the activities referenced in paragraph 188 would actively induce direct infringement of the '537 patent. On information and belief, despite such knowledge, Health Net has been and is actively inducing the infringement of the '537 patent by others, and is doing do willfully and deliberately.

193. On information and belief, Health Net will continue to induce infringement of the '537 patent unless and until enjoined by the Court.

194. As a result of Health Net's inducement of infringement of the '537 patent, Plaintiffs have suffered damages.

COUNT V

(Infringement of the '077 Patent Under 35 U.S.C. § 271(b) by Health Net)

195. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

196. On information and belief, by covering and/or directing or providing payment for others' use of the Hikma Defendants' generic version of VASCEPA® for the CV Indication, Health Net has been and is inducing others to use, offer to sell, sell, or otherwise promote and distribute the Hikma Defendants' generic version of VASCEPA® to reduce triglycerides in a subject with mixed dyslipidemia by administering about 4 g of ethyl eicosapentaenoate per day, thereby infringing the '077 patent.

197. On information and belief, healthcare providers administering and/or patients using 4 g per day of the Hikma Defendants' generic version of VASCEPA® capsules within the United States do so, among other reasons, to reduce fasting triglyceride and hs-CRP levels in patients with mixed dyslipidemia, and thus directly infringe at least claim 8 of the '077 patent.

198. On information and belief, Health Net possessed the specific intent to encourage direct infringement of the '077 patent. On information and belief, Health Net knew about the '077 patent at least as of when the Hikma Defendants' generic version of VASCEPA® was launched with a label listing only the Severe Hypertriglyceridemia Indication; and/or when Amarin announced the filing of this lawsuit against the Hikma Defendants; and/or when Amarin sent a letter to payers, including Health Net's contracted Pharmacy Benefit Manufacturer Envolve, informing them of the filing of the patent exclusivity for the CV Indication and about this lawsuit against the Hikma Defendants, and before performing the activities referenced in paragraph 196. In the alternative, Health Net knows about the '077 patent at least as of the filing of this Amended Complaint and continues the activities referenced in paragraph 196.

199. Alternatively, Health Net subjectively believed that there was a high probability that the administration and use of 4 g per day of the Hikma Defendants' generic version of VASCEPA® for reducing fasting triglyceride and hs-CRP levels in subjects with mixed

dyslipidemia was protected by a valid patent, and that the activities referenced in paragraph 196 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded itself to the infringing nature of the use and sale of the Hikma Defendants' generic version of VASCEPA®.

200. On information and belief, Health Net knew that the administration or use of the Hikma Defendants' generic version of VASCEPA® would include for daily administration of a 4 g/day dose to reduce fasting triglyceride and hs-CRP levels in subjects with mixed dyslipidemia, and so would be an act of direct infringement of the '077 patent, and that the activities referenced in paragraph 196 would actively induce direct infringement of the '077 patent. On information and belief, despite such knowledge, Health Net has been and is actively inducing the infringement of the '077 patent by others, and is doing do willfully and deliberately.

201. On information and belief, Health Net will continue to induce infringement of the '077 patent unless and until enjoined by the Court.

202. As a result of Health Net's inducement of infringement of the '077 patent, Plaintiffs have suffered damages.

COUNT VI

(Infringement of the '861 Patent Under 35 U.S.C. § 271(b) by Health Net)

203. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

204. On information and belief, by covering and/or directing or providing payment for others' use of the Hikma Defendants' generic version of VASCEPA® for the CV Indication, Health Net has been and is inducing others to use, offer to sell, sell, or otherwise promote and distribute the Hikma Defendants' generic version of VASCEPA® to reduce the risk of a cardiovascular death in a subject with established cardiovascular disease, including subjects with

a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL, by administering about 4 g of ethyl icosapentate per day for a period effective to reduce risk of cardiovascular death, thereby infringing the ’861 patent.

205. On information and belief, healthcare providers administering and/or patients using 4 g per day of the Hikma Defendants’ generic version of VASCEPA® capsules within the United States do so, among other reasons, to reduce the risk of cardiovascular death in patients with established cardiovascular disease, including the patient population recited in claims 1 and 2, and thus directly infringe at least claim 1 and 2 of the ’861 patent.

206. On information and belief, Health Net possessed the specific intent to encourage direct infringement of the ’861 patent. On information and belief, Health Net knew about the ’861 patent at least as of when the Hikma Defendants’ generic version of VASCEPA® was launched with a label listing only the Severe Hypertriglyceridemia Indication; and/or when Amarin announced the filing of this lawsuit against the Hikma Defendants; and/or when Amarin sent a letter to payers, including Health Net’s contracted Pharmacy Benefit Manufacturer Envolve, informing them of the filing of the patent exclusivity for the CV Indication and about this lawsuit against the Hikma Defendants, and before performing the activities referenced in paragraph 204. In the alternative, Health Net knows about the ’861 patent at least as of the filing of this Amended Complaint and continues the activities referenced in paragraph 204.

207. Alternatively, Health Net subjectively believed that there was a high probability that the administration and use of 4 g per day of icosapent ethyl capsules for reducing risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline

LDL-C level of about 40 mg/dL to about 100 mg/dL, for a period effective to reduce risk of cardiovascular death, was protected by a valid patent, and that the activities referenced in paragraph 204 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded itself to the infringing nature of the use and sale of the Hikma Defendants' generic version of VASCEPA®.

208. On information and belief, Health Net knew that the administration or use of the Hikma Defendants' generic version of VASCEPA® would include daily administration of a 4 g/day dose to reduce risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL, for a period effective to reduce risk of cardiovascular death, and so would be an act of direct infringement of the '861 patent, and that the activities referenced in paragraph 204 would actively induce direct infringement of the '861 patent. On information and belief, despite such knowledge, Health Net has been and is actively inducing the infringement of the '861 patent by others, and is doing do willfully and deliberately.

209. On information and belief, Health Net will continue to induce infringement of the '861 patent unless and until enjoined by the Court.

210. As a result of Health Net's inducement of infringement of the '861 patent, Plaintiffs have suffered damages.

JURY TRIAL DEMAND

Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiffs hereby demand a trial by jury of all issues so triable.

PRAYER FOR RELIEF

Plaintiffs respectfully pray for the following relief:

a) Enter judgment that the Hikma Defendants have induced the infringement of the '537, '077, and '861 patents by making, selling, offering to sell and importing generic icosapent ethyl capsules in or into the United States;

b) Enter judgment that Health Net has induced the infringement of the '537, '077, and '861 patents by covering and/or providing payment for others' use, offer to sell, or sale of the Hikma Defendants' generic version of VASCEPA® in the United States;

c) Enter judgment that Defendants' infringement of the '537, '077, and '861 patents has been and is willful;

d) Issue an injunction under 35 U.S.C. § 283 permanently enjoining all Defendants, their officers, agents, servants, employees, licensees, representatives, and attorneys, and all other persons acting or attempting to act in active concert or participation with them or acting on their behalf, from, directly or indirectly, making, selling, offering to sell, and importing into the United States any drug product for a use that is covered by the '537, '077, and '861 patents;

e) Award Plaintiffs damages in an amount sufficient to compensate them for Defendants' infringement of the '537, '077, and '861 patents, together with prejudgment and post-judgment interests and costs under 35 U.S.C. § 284;

f) Declare this to be exceptional case under 35 U.S.C. § 285 and award Plaintiffs their reasonable attorneys' fees, expenses, and costs incurred in this action;

g) Perform an accounting of Defendants' infringing activities through trial and judgment; and

h) Award Plaintiffs such other and further relief as this Court deems just and proper.

Dated: January 25, 2021

FISH & RICHARDSON P.C.

By: */s/ Jeremy D. Anderson*

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