ANDA 209457

ANDA APPROVAL

Hikma Pharmaceuticals USA Inc.
1809 Wilson Road
Columbus, OH 43228
Attention: Jerald Andry, PharmD, MS
Senior Director, Drug Regulatory Affairs and Medical Affairs

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on July 26, 2016, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Icosapent Ethyl Capsules, 1 gram.

Reference is also made to the complete response letter issued by this office on June 10, 2019, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act. Accordingly, the ANDA is **approved**, effective on the date of this letter. We have determined your Icosapent Ethyl Capsules, 1 gram, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Vascepa Capsules, 1 gram, of Amarin Pharmaceuticals Ireland, Limited (Amarin).

The RLD upon which you have based your ANDA, Amarin's Vascepa Capsules, 1 gram, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
8,293,727 (the '727 patent)	February 9, 2030
8,293,728 (the '728 patent)	February 9, 2030
8,298,554 (the '554 patent)	April 29, 2030
8,314,086 (the '4,086 patent)	February 9, 2030
8,318,715 (the '715 patent)	February 9, 2030

8,357,677 (the '677 patent)	February 9, 2030
8,367,652 (the '652 patent)	February 9, 2030
8,377,920 (the '920 patent)	February 9, 2030
8,399,446 (the '446 patent)	February 9, 2030
8,410,086 (the '0,086 patent)	June 15, 2030
8,415,335 (the '335 patent)	February 9, 2030
8,426,399 (the '399 patent)	February 9, 2030
8,431,560 (the '560 patent)	February 9, 2030
8,440,650 (the '650 patent)	February 9, 2030
8,445,003 (the '003 patent)	April 29, 2030
8,445,013 (the '013 patent)	April 29, 2030
8,454,994 (the '994 patent)	April 29, 2030
8,455,472 (the '472 patent)	June 15, 2030
8,501,225 (the '225 patent)	April 29, 2030
8,518,929 (the '929 patent)	February 9, 2030
8,524,698 (the '698 patent)	February 9, 2030
8,546,372 (the '372 patent)	February 9, 2030
8,551,521 (the '521 patent)	April 29, 2030
8,563,608 (the '608 patent)	April 29, 2030
8,617,593 (the '593 patent)	April 29, 2030
8,617,594 (the '594 patent)	April 29, 2030
8,618,166 (the '166 patent)	April 29, 2030
8,623,406 (the '406 patent)	April 29, 2030

8,642,077 (the '077 patent)	April 29, 2030
8,669,245 (the '245 patent)	June 15, 2030
8,680,144 (the '144 patent)	February 9, 2030
8,691,871 (the '871 patent)	April 29, 2030
8,703,185 (the '185 patent)	April 29, 2030
8,709,475 (the '475 patent)	April 29, 2030
8,710,041 (the '041 patent)	June 15, 2030
9,198,892 (the '892 patent)	September 25, 2027
9,603,826 (the '826 patent)	June 28, 2033
9,610,272 (the '272 patent)	June 28, 2033
9,623,001 (the '001 patent)	June 28, 2033
9,693,984 (the '984 patent)	June 28, 2033
9,693,985 (the '985 patent)	June 28, 2033
9,693,986 (the '986 patent)	June 28, 2033
9,700,537 (the '537 patent)	May 31, 2027
9,918,954 (the '954 patent)	June 28, 2033
10,010,517 (the '517 patent)	April 29, 2030
10,265,287 (the '287 patent)	April 29, 2030
10,278,935 (the '935 patent)	June 28, 2033
10,278,936 (the '936 patent)	June 28, 2033
10,278,937 (the '937 patent)	June 28, 2033
10,383,840 (the '840 patent)	June 28, 2033
10,555,924 (the '924 patent)	June 28, 2033

10,555,925 (the '925 patent)	June 28, 2033
10,568,861 (the '861 patent)	June 28, 2033
10,576,054 (the '054 patent)	June 28, 2033

With respect to: 1) the '593 patent insofar as pertains to U-2691 (use of Vascepa to treat hypertriglyceridemia in an adult patient with elevated triglyceride (TG) levels (>= 150 mg/dL) and on statin therapy); 2) the '406 patent insofar as it pertains to U-2692 (use of Vascepa to reduce triglycerides in an adult patient with elevated triglyceride (TG) levels (>= 150 mg/dL) and on statin therapy); and 3) the '0,086, '994, '472, '166, '077, '245, '144, '871, '185, '475, '041, '892, '826, '272, '001, '984, '985, '986, '537, '954, '517, '287, '935, '936, '937, '840, '924, '925, '861, and '054 patents, your ANDA contains statements under section 505(j)(2)(A)(viii) of the FD&C Act that these are method-of-use patents that do not claim any indication or other conditions of use for which you are seeking approval under your ANDA.

With respect to: 1) the '593 patent insofar as pertains to U-1478 (method of reducing TG levels in patient on statin therapy suffering from severe hypertriglyceridemia); 2) the '406 patent insofar as it pertains to U-1478 (method of reducing TG levels in patient on statin therapy suffering from severe hypertriglyceridemia); and 3) the '727, '728, '554, '4,086, '715, '677, '652, '920, '446, '335, '399, '560, '650, '003, '013, '225, '929, '698, '372, '521, '608, and '594 patents, your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Icosapent Ethyl Capsules, 1 gram, under this ANDA. You have notified the Agency that Hikma Pharmaceuticals USA Inc. (Hikma) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. Litigation was initiated within the statutory 45-day period against Hikma for infringement of the '728, '715, '677, '652, '920, '446, '335, '399, '560, '650, '929, '698, '372, and '594 patents in the United States District Court for the District of Nevada [Amarin Pharma, Inc., *et al.*, v. Hikma Pharmaceuticals USA, Inc., *et al.*, Civil Action No. 16-02525]. You have also notified the Agency that, on March 30, 2020, the court ordered that all of the asserted claims are invalid as obvious.[1]

With respect to 180-day generic drug exclusivity, we note that Hikma was one of the first ANDA applicants for Icosapent Ethyl Capsules, 1 gram, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Hikma may be eligible for 180 days of shared generic drug exclusivity for Icosapent Ethyl Capsules, 1 gram. This exclusivity, which is provided for under 505(j)(5)(B)(iv) of the FD&C Act, would begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). The Agency notes that Hikma failed to obtain tentative approval of its ANDA within 30 months after the date on which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). The Agency is not, however, making a formal determination at this time of Hikma's eligibility for 180-day generic drug exclusivity. It will do so only if a subsequent paragraph IV applicant becomes eligible for full approval (a) within 180 days after Hikma

or any first applicant begins commercial marketing of Icosapent Ethyl Capsules, 1 gram, or (b) at any time prior to the expiration of the '593, '406, '727, '728, '554, '4,086, '715, '677, '652, '920, '446, '335, '399, '560, '650, '003, '013, '225, '929, '698, '372, '521, '608, and '594 patents, if Hikma or any first applicant has not begun commercial marketing. Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see: http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[2] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts.

All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at: http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at:

https://www.fda.gov/media/71211/download. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

For Vincent Sansone, PharmD
CAPT, USPHS
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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[1] We note that you also provided documentation that, prior to trial, the parties agreed to reduce the number of claims asserted at trial to a subset of the originally asserted patents, i.e., certain claims of the '728, '715, '677, '652, '560, and '929 patents.

[2] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

John Ibrahim

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