ANDA 209525

ANDA TENTATIVE APPROVAL

Teva Pharmaceuticals USA, Inc.
400 Interpace Parkway, Building A
Parsippany, NJ 07054
Attention: Elisabeth Gray
Director, Regulatory Affairs, US Generics

Dear Madam:

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, 500 mg and 1 gram.

Reference is also made to the complete response letter issued by this office on August 24, 2018, 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. We have determined your Icosapent Ethyl Capsules, 500 mg and 1 gram, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Vascepa Capsules, 500 mg and 1 gram, of Amarin Pharmaceuticals Ireland, Limited (Amarin).

However, we are unable to grant final approval to your ANDA at this time because of the exclusivity issue noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the Agency at this time (e.g., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the FD&C Act.

The RLD upon which you have based your ANDA, Amarin's Vascepa Capsules, 500 mg and 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 (1 gram strength only)
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 (1 gram strength only)
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 (1 gram strength only)
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

Your ANDA contains paragraph IV certifications to each of the patents**Error! Reference source not found.** 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, 500 mg and 1 gram, under this ANDA. You have notified the Agency that Teva Pharmaceuticals USA, Inc. (Teva) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. With respect to Icosapent Ethyl Capsules, 1 gram, litigation was initiated within the statutory 45-day period against Teva 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. and Amarin Pharmaceuticals Ireland Limited v. Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Limited, Civil Action No. 16-02658]. With respect to Icosapent Ethyl Capsules, 500 mg, litigation was initiated within the statutory 45-day period against Teva for infringement of the '728, '715, '677, '652, '920, '335, '399, '650, '929, '698, '372, and '594 patents in the United States District Court for the District of Nevada [Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited v. Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Limited, Civil Action No. 17-02641]. You have also notified the Agency that these cases were consolidated with Civil Action No. 16-02525, and that this case was dismissed.

The RLD upon which you have based your ANDA, Amarin's Vascepa Capsules, 500 mg and 1 gram, is also subject to a period of exclusivity. As noted in the Orange Book, the I-819 exclusivity is scheduled to expire on December 13, 2022. Your ANDA contains a statement that you do not seek to market your Icosapent Ethyl Capsules, 500 mg and 1 gram, prior to the expiration of the I-819 exclusivity. Therefore, final approval cannot be granted until the exclusivity has expired, currently December 13, 2022.

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.

RESUBMISSION

To request final approval, please submit an amendment titled "FINAL APPROVAL REQUESTED" with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 3 months for Agency review. Accordingly, such a request for final approval should be submitted no later than 3 months prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in the status of the manufacturing and testing facilities' compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. As part of this consideration, applicants should monitor any changes to the RLD that occur after tentative approval, including changes in labeling, patent or exclusivity information, or marketing status. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a "FINAL APPROVAL REQUESTED"

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to December 13, 2022, you should amend your ANDA accordingly.

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.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Christopher Jacobs, Regulatory Project Manager, at (240) 402 - 9946.

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] With respect to both strengths, the Agency notes that the '0,086, '994, '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 were submitted to the Agency after submission of your ANDA. In addition, with respect to the 1 gram strength, the Agency notes that the '472 and '166 patents were submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.

[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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