



ANDA 090165

ANDA APPROVAL

Zydus Pharmaceuticals (USA), Inc.
73 Route 31 North
Pennington, NJ 08534
Attention: Srinivas Gurram
Vice President and Head Regulatory Affairs

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on November 28, 2007, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Aripiprazole Orally Disintegrating Tablets USP, 10 mg, 15 mg, 20 mg, and 30 mg.¹

Reference is also made to the tentative approval letter issued by this office on July 27, 2012, the complete response letter issued by this office on March 2, 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 is safe and effective for use as recommended in the submitted labeling. Accordingly, the ANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Aripiprazole Orally Disintegrating Tablets USP, 10 mg, 15 mg, 20 mg, and 30 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Abilify DISCMELT Orally Disintegrating Tablets, 10 mg, 15 mg, 20 mg, and 30 mg, of Otsuka Pharmaceutical Company, Ltd. (Otsuka).

The RLD upon which you have based your ANDA, Otsuka’s Abilify DISCMELT Orally Disintegrating Tablets, 10 mg, 15 mg, 20 mg, and 30 mg, 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>U.S. Patent Number</u>	<u>Expiration Date</u>
7,053,092 (the '092 patent)	January 28, 2022
8,017,615 (the '615 patent)	December 16, 2024*
8,518,421 (the '421 patent)	July 24, 2021*
8,580,796 (the '796 patent)	March 25, 2023*
8,642,600 (the '600 patent)	July 28, 2022*
8,642,760 (the '760 patent)	March 25, 2023*
8,759,350 (the '350 patent)	March 2, 2027 (10 mg and 15 mg strengths only)
9,089,567 (the '567 patent)	January 28, 2022 (10 mg and 15 mg strengths only)
9,125,939 (the '939 patent)	July 28, 2026 (10 mg and 15 mg strengths only)
9,358,207 (the '207 patent)	April 12, 2020

9,359,302 (the '302 patent)	September 25, 2022
9,387,182 (the '182 patent)	December 25, 2023

* with pediatric exclusivity added

With respect to the '615, '421, '796, '760, '567, '207, and '302 (excluding acute treatment of manic and mixed episodes associated with bipolar I disorder, adjunctive treatment of major depressive disorder, and treatment of irritability associated with autistic disorder) patents,² 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 Aripiprazole Orally Disintegrating Tablets USP, 10 mg, 15 mg, 20 mg, and 30 mg, under this ANDA. You have notified the Agency that Zydus Pharmaceuticals (USA), Inc. (Zydus) complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and that litigation was initiated for infringement of the '615, '421, '796, and '760 patents in the United States District Court for the District of New Jersey [Otsuka Pharmaceutical Co., Ltd. v. Zydus Pharmaceuticals USA Inc. and Cadila Healthcare Limited, Civil Action No. 14-03168], for infringement of the '567 patent in the United States District Court for the District of New Jersey [Otsuka Pharmaceutical Co., Ltd. v. Zydus Pharmaceuticals USA Inc. and Cadila Healthcare Limited, Civil Action No. 15-07802], and for infringement of the '302 patent in the United States District Court for the District of New Jersey [Otsuka Pharmaceutical Co., Ltd. v. Zydus Pharmaceuticals USA Inc. and Cadila Healthcare Limited, Civil Action No. 16-07705]. You have also notified the Agency that these cases were dismissed.

With respect to the '092, '600, '350, '939, '182, and '302 (acute treatment of manic and mixed episodes associated with bipolar I disorder, adjunctive treatment of major depressive disorder, and treatment of irritability associated with autistic disorder only) 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 for which you are seeking approval under your ANDA.

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 506l 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 506l(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 provisions³ 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 <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

For Vincent Sansone, Pharm.D.
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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- ¹ We note that the reference listed drug (RLD) upon which you have based this ANDA, Otsuka Pharmaceutical Company, Ltd.'s (Otsuka's) Abilify DISCMELT Orally Disintegrating Tablets, 10 mg, 15 mg, 20 mg, and 30 mg, are no longer being marketed in the United States and are currently listed in the discontinued section of FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"). The Agency has determined that Otsuka's Abilify DISCMELT Orally Disintegrating Tablets, 10 mg, 15 mg, 20 mg, and 30 mg, were not withdrawn from sale for reasons of safety or effectiveness. FDA published this determination in the *Federal Register* (see 82 FR 19735; April 28, 2017 for the 10 mg and 15 mg strengths, and 74 FR 63404; December 3, 2009 for the 20 mg and 30 mg strengths). This determination allows the Agency to approve ANDAs for the discontinued drug products.
 - ² The Agency notes that the '092, '615, '421, '796, '600, '760, '350, '567, '939, '207, '302, and '182 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.
 - ³ Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).



Sarah
Kurtz

Digitally signed by Sarah Kurtz
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