DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 206726

ANDA APPROVAL

Mylan Pharmaceuticals, Inc.
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504
Attention: Juliane M. Foley
Director, Regulatory Affairs

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA), submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for Methylphenidate Hydrochloride Extended-Release Tablets USP, 18 mg, 27 mg, 36 mg, and 54 mg.

Reference is also made to the complete response letter issued by this office on July 31, 2015, and to your amendments dated February 29, May 23, and July 22, 2016.

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 Methylphenidate Hydrochloride Extended-Release Tablets USP, 18 mg, 27 mg, 36 mg, and 54 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Concerta Extended-Release Tablets, 18 mg, 27 mg, 36 mg, and 54 mg, of Janssen Pharmaceuticals, Inc. (Janssen).

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The "interim" dissolution specifications are as follows.

USP Apparatus	7	
Rotational Speed	30 cycles/min; 2-3 cm amplitude	
Temperature	37 ± 0.5 °C	
Media	Acidified water. Adjust with phosphoric acid to a pH of 3	
Volume	50 mL	
Specifications	Time (h)	Amount Dissolved
	1	(b) (4) %
	4	(b) (4) %
	10	NLT (b) (4) %
	Average from 3 to 6 h: (b) (4) *	

*The average percentage released from 3 to 6 h should be calculated as: *(Y - X)/3*
Y = cumulative drug released from 0 to 6 h
X = cumulative drug released from 0 to 3 h

The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data for the first three production size batches. Data should be submitted as a Special Supplement – Changes Being Effected when there are no revisions to the "interim" specifications or when the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The RLD upon which you have based your ANDA, Janssen's Concerta Extended-Release Tablets, 18 mg, 27 mg, 36 mg, and 54 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.S. Patent Number	Expiration Date
6,919,373 (the '373 patent)	January 31, 2018*
6,930,129 (the '129 patent)	January 31, 2018*
8,163,798 (the '798 patent)	January 31, 2018*
8,629,179 (the '179 patent)	January 31, 2018*
9,000,038 (the '038 patent)	January 31, 2018*
9,029,416 (the '416 patent)	July 31, 2017
9,144,549 (the '549 patent)	July 31, 2017

(*with pediatric exclusivity added)

Your ANDA contains paragraph IV certifications to each of the patents 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 Methylphenidate Hydrochloride Extended-Release Tablets USP, 18 mg, 27 mg, 36 mg, and 54 mg, under this ANDA.[1] You have notified the agency that Mylan Pharmaceuticals, Inc. (Mylan) complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and that litigation was initiated against Mylan for infringement of the '798 patent within the statutory 45-day period in the United States District Court for the District of Delaware [Alza Corporation and Janssen Pharmaceuticals, Inc. v. Mylan Pharmaceuticals, Inc. and Mylan, Inc., Civil Action No. 14-cv-00594] and in the United States District Court for the Northern District of West Virginia [Alza Corporation and Janssen Pharmaceuticals, Inc. v. Mylan Pharmaceuticals, Inc. and Mylan, Inc., Civil Action No. 14-cv-00085]. You have further notified the agency that the first case has been dismissed and the second case was resolved by consent judgment that expressly did not restrict FDA from approving this ANDA.

With respect to 180-day exclusivity, the drug product approved in this ANDA is subject to the statutory provisions related to 180-day exclusivity in place prior to the *Medicare Prescription*

[1] We note that the '179, '038, '416, and '549 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.

Drug, Improvement, and Modernization Act of 2003 (MMA).[2] There is one remaining patent on which exclusivity potentially could be based, the '179 patent.[3] With respect to the '179 patent, we note another ANDA applicant for Methylphenidate Hydrochloride Extended-Release Tablets USP, 18 mg, 27 mg, 36 mg, and 54 mg provided a paragraph IV certification to the '179 patent prior to Mylan's paragraph IV certification. However, Mylan brought a declaratory judgment action against Janssen with respect to the '179 patent in the United States District Court for the Eastern District of Pennsylvania [Mylan Pharmaceuticals Inc. v. Janssen Pharmaceuticals, Civil Action No. 2:15-cv-02990-MAK]. On October 16, 2015, the court ruled that the '179 patent is not infringed by Mylan's product and this decision was not appealed.[4] Under the applicable 180-day exclusivity provisions, this order triggered the first applicant's 180-day generic drug exclusivity period associated with the '179 patent.[5]

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 & 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.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration

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[2] Specifically, because another ANDA for Methylphenidate Hydrochloride Extended-Release Tablets USP, 18 mg, 27 mg, 36 mg, and 54 mg was filed before the date of enactment of the *Medicare Prescription Drug, Improvement and Modernization Act* (MMA) (Public Law 108-173) on December 8, 2003, references to the 180-day exclusivity provisions are to the section of the FD&C Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1); see also Letter to Applicant fr. G. Buehler, Office of Generic Drugs (April 15, 2009) (regarding Topiramate Sprinkle Capsules, reflecting FDA's interpretation of section 1102(b)(1) of the MMA)). This correspondence is currently available on FDA's website at http://www fda.gov/downloads/AboutFDA/CentersOffices/CenterforDrugEvaluationandResearch/UCM135323.pdf.

[3] Exclusivity based on the '129, '798, '038, '416, and '549 patents previously has been triggered and has run by a first applicant's marketing of an authorized generic. See, e.g., FDA Citizen Petition Response, at 7, FDA Docket No. 2000P-1446 (Feb. 6, 2001) (finding Mylan's marketing of an authorized generic of Pfizer's nifedipine product triggered Mylan's 180-day exclusivity period) (upheld in *Mylan Pharmaceuticals, Inc. v. Thompson*, 207 F. Supp. 2d 476 (N.D.W.Va. 2001)). Exclusivity based on the '373 was triggered by a decision of the U.S. Court of Appeals for the Federal Circuit and has run. See Alza Corp. v. Andrx Pharms. LLC, 603 F.3d 935, 944 (Fed. Cir. 2010).

[4] Final Judgment, at 3, *Mylan Pharms., Inc. v. Janssen Pharms., Inc.,* Civil Action No. 15-cv-02990 (Oct. 16, 2015).

[5] See note 1 above, and Section 505(j)(5)(B)(iv) of the FD&C Act (in which 180-day exclusivity is triggered by the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv)).

Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions 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 1 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.

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}

Carol A. Holquist, RPh
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

Carol Holquist

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