



ANDA 202578

ANDA APPROVAL

Mylan Pharmaceuticals
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310
Attention: Joseph J. SobECKi
Vice President, Regulatory Affairs

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated November 30, 2010, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Guanfacine Extended-release Tablets, 1 mg, 2 mg, 3 mg, and 4 mg.

Reference is also made to your amendments dated January 9 and July 30, 2014; and March 4 and April 8, 2015. The January 9, 2014 submission constituted a complete response to our November 22, 2013 action letter.

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 Division of Bioequivalence has determined your Guanfacine Extended-release Tablets, 1 mg, 2 mg, 3 mg, and 4 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Intuniv Tablets, 1 mg, 2 mg, 3 mg, and 4 mg, of Shire. 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:

Medium: pH 2.2 HCl Buffer
Volume: 900 mL
Apparatus: USP apparatus 2 (paddles)
Speed: 75 rpm

| Time | Specifications |
|-------|----------------|
| 1 hr | (b) (4) % |
| 4 hr | (b) (4) % |
| 8 hr | (b) (4) % |
| 16 hr | NLT (b) (4) % |

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 reference listed drug (RLD) upon which you have based your ANDA, Shire’s Intuniv Tablets, 1 mg, 2 mg, 3 mg, and 4 mg, is subject to periods of patent protection. The following patents and expiration dates (with pediatric exclusivity added) 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> |
|-----------------------------|------------------------|
| 5,854,290 (the '290 patent) | March 21, 2016 |
| 6,287,599 (the '599 patent) | June 20, 2021 |
| 6,811,794 (the '794 patent) | January 4, 2023 |

Your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each of these patents is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Guanfacine Extended-release Tablets, 1 mg, 2 mg, 3 mg, and 4 mg, under this ANDA. You have notified the agency Mylan Pharmaceuticals Inc. (Mylan) complied with the requirements of section 505(j)(2)(B) of the Act, and litigation for infringement of the '290, '599 and '794 patents was brought against Mylan within the statutory 45-day period in the United States District Court for the Southern District of New York and Northern District of West Virginia [Shire LLC v. Mylan Pharmaceuticals Inc., Civil Action Nos. 11-cv-2024 and 11-cv-0201]. You have notified the Agency that the New York case was dismissed and a consent judgment was entered in the West Virginia case.

Under section 506A of the 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 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
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,

William P. Rickman

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

Digitally signed by William P. Rickman -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA,
ou=People, 0.9.2342.19200300.100.1.1=1300043242,
cn=William P. Rickman -S
Date: 2015.06.02 07:57:32 -04'00'