

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the “listed drug,” which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the “Approved Drug Products With Therapeutic Equivalence Evaluations,” which is known generally as the “Orange Book.” Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

SYMMETREL (amantadine hydrochloride), Syrup, 50 mg/5 mL, is the subject of NDAs 016023 and 017118, held by Endo Pharmaceuticals, and initially approved on February 14, 1968, and July 20, 1976, respectively. SYMMETREL is indicated for the prophylaxis and treatment of signs and symptoms of infection caused by various strains of influenza A virus. SYMMETREL is also indicated for the treatment of parkinsonism and drug-induced extrapyramidal reactions.

In a letter dated March 19, 2009, Endo Pharmaceuticals notified FDA that SYMMETREL (amantadine hydrochloride), Syrup, 50 mg/5 mL, was being discontinued and requested withdrawal of NDA016023 for that product. FDA moved the drug product to the “Discontinued Drug Product List” section of the Orange Book and announced in the **Federal Register** of July 21, 2010 (75 FR 42455), that FDA was withdrawing approval of NDA 016023, effective August 20, 2010.

Hyman, Phelps & McNamara submitted a citizen petition dated August 3, 2016 (Docket No. FDA-2016-P-2469), under 21 CFR 10.30, requesting that the Agency determine whether SYMMETREL (amantadine hydrochloride), Syrup, 50 mg/5 mL, was withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that SYMMETREL (amantadine hydrochloride), Syrup, 50 mg/5 mL, was not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that this drug product was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of SYMMETREL (amantadine hydrochloride), Syrup, 50 mg/5 mL, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have reviewed the available evidence and determined that this drug product was not withdrawn from sale for reasons of safety or effectiveness.¹

Accordingly, the Agency will continue to list SYMMETREL (amantadine hydrochloride), Syrup, 50 mg/5 mL, in the “Discontinued Drug Product List” section of the Orange Book. The “Discontinued Drug Product List” delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. FDA will not begin procedures to withdraw approval of approved ANDAs that refer

¹ Due to high levels of resistance to currently circulating Influenza A viruses, the Centers for Disease Control and Prevention currently recommends against using amantadine to treat Influenza A. Given the potential for viral reassortment, however, amantadine may be effective against future Influenza A viruses. Consistent with this, the current label for SYMMETREL (amantadine hydrochloride), Syrup, 50 mg/5 mL, was revised to caution prescribers to consider susceptibility and clinical benefit when deciding whether to use amantadine to treat Influenza A.

to SYMMETREL. Additional ANDAs that refer to SYMMETREL (amantadine hydrochloride), Syrup, 50 mg/5 mL, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: January 12, 2017.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2017-01064 Filed 1-17-17; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2010-D-0026]

Assessment of Abuse Potential of Drugs; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a guidance for industry entitled “Assessment of Abuse Potential of Drugs.” This guidance is intended to assist sponsors of investigational new drugs and applicants for approval of a new drug in evaluating whether their new drug product has abuse potential. Specifically, this guidance provides recommendations for assessing the abuse potential of central nervous system (CNS)-active new drugs. Drug products with abuse potential generally contain drug substances that are active within the CNS and produce psychoactive effects such as euphoria and hallucinations. Thus, if a drug substance is CNS-active, the new drug product containing that drug substance will likely need to undergo a thorough assessment of its abuse potential and may be subject to control under the Controlled Substances Act (CSA). This guidance finalizes the draft guidance of the same name issued on January 27, 2010.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- **Mail/Hand delivery/Courier (for written/paper submissions):** Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2010-D-0026 for "Assessment of Abuse Potential of Drugs; Guidance for Industry; Availability." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- **Confidential Submissions—**To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS

CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Dominic Chiapperino, Controlled Substance Staff, Center for Drug Evaluation and Research, Bldg. 51, Rm. 5148, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993, 301-796-1183.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Assessment of Abuse Potential of Drugs." Under the Federal Food, Drug, and Cosmetic Act, an abuse potential assessment is part of the general evaluation of the safety and efficacy of a new drug to be used under medical

supervision. Additionally, if a new drug has abuse potential, the Secretary of Health and Human Services (HHS) is required under the CSA (21 U.S.C. 801 *et seq.*) to make a recommendation for scheduling to the Drug Enforcement Administration (DEA). The regulatory responsibilities for this process are described in Title 21, United States Code (U.S.C.) 811. FDA, in consultation with the National Institute on Drug Abuse (NIDA) conducts the medical and scientific analysis on behalf of HHS. Specifically, the Controlled Substance Staff of FDA performs this scientific evaluation of the abuse potential of a drug for FDA, in consultation with NIDA, as described in a Memorandum of Understanding (MOU) of March 8, 1985 (50 FR 9518) (available at: <http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm116365.htm>). When an applicant submits a New Drug Application (NDA) for a drug with abuse potential to FDA for review, the applicant is required to propose a CSA schedule for the new drug (21 CFR 314.50(d)(5)(vii)). The applicant's proposal is considered by the Agency during its evaluation of the drug's abuse potential. FDA prepares a scientific analysis with a recommendation for scheduling the drug under the CSA, as warranted, based on consideration of all relevant and available data. This recommendation is forwarded by the HHS Assistant Secretary for Health to DEA for their consideration in the decision on final scheduling of the drug.

Under new legislation enacted in 2015, the Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114-89), upon receipt of both: (1) Notification from FDA that a marketing application has been approved by FDA and (2) the scheduling recommendation of HHS with respect to the subject drug in the marketing application, DEA shall within 90 days schedule the drug by rulemaking, thus establishing the effective date of approval for the drug product. See 21 U.S.C. 355(x); see also Public Law 114-89 (November 25, 2015). Control under Schedules II, III, IV, or V results in schedule-specific regulatory requirements relating to the drug's labeling, prescribing, dispensing, advertising, manufacturing, distribution, importation/exportation, promotion, marketing, and legitimate use in medical treatment. See generally 21 U.S.C. 821-831 and 21 CFR 1300-1321. Scheduling of a substance in the CSA is for the purpose of reducing abuse and diversion.

This guidance provides important recommendations to sponsors, applicants, and potential applicants in the approaches to collecting data that should comprise the abuse potential assessment submitted in the marketing application to FDA if one is required pursuant to § 314.50(d)(5)(vii).

In the **Federal Register** of January 27, 2010 (75 FR 4400), FDA issued the draft guidance for industry “Assessment of Abuse Potential of Drugs.” Based on the 2010 draft guidance, and consideration of comments received from the public, this guidance provides the Agency’s current thinking with respect to the scientific methods recommended to assess abuse potential. The guidance also adds more detailed discussion about key questions and decision points to consider during drug development that will likely determine the appropriate studies for sponsors and applicants to conduct to address the abuse potential of their new drug, inform appropriate labeling of the product upon its approval, and allow a thorough scientific and medical evaluation to support scheduling decisions in accordance with the CSA. In addition, this guidance takes into consideration other guidance issued and legislation enacted since 2010.

This guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on assessment of abuse potential of drugs. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collection of information in part 314, including § 314.50(d)(5)(vii), has been approved under OMB control number 0910–0001. The collection of information in 21 CFR part 312 for investigational drugs has been approved under OMB control number 0910–0014. The collection of information in the guidance “Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products” has been approved under OMB control number 0910–0429. The collection of information in 21 CFR 201.56 and 201.57, prescription drug labeling, has been approved under OMB control number 0910–0572. The collection of information in 21 CFR part

58, Good Laboratory Practice for Nonclinical Studies, has been approved under OMB control number 0910–0119.

III. Electronic Access

Persons with access to the Internet may obtain the guidance at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <https://www.regulations.gov>.

Dated: January 12, 2017.

Leslie Kux,

Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2017–D–0113]

The Prohibition of Distributing Free Samples of Tobacco Products; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “The Prohibition of Distributing Free Samples of Tobacco Products; Draft Guidance for Industry.” The draft guidance, when finalized, would provide information intended to assist manufacturers, distributors, and retailers in complying with the regulations prohibiting the distribution of free samples of tobacco products.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by February 17, 2017.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are

solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else’s Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”).

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- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA–2017–D–0113 for “The Prohibition of Distributing Free Samples of Tobacco Products.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

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