



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-P-2469]

Determination That SYMMETREL (Amantadine Hydrochloride), Syrup, 50 milligrams/5 Milliliters, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has determined that SYMMETREL (amantadine hydrochloride), Syrup, 50 milligrams/5 milliliters (50 mg/5 mL), was not withdrawn from sale for reasons of safety or effectiveness. This determination means that FDA will not begin procedures to withdraw approval of abbreviated new drug applications (ANDAs) that refer to SYMMETREL, and it will allow FDA to continue to approve ANDAs that reference SYMMETREL if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: Stefanie S. Kraus, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6215, Silver Spring, MD 20993-0002, 301-796-9585.

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approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).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may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness.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

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.

refer 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.

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