4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA-2014-P-0637, FDA-2014-P-0315]

Determination That FUSILEV (Levoleucovorin Calcium), Injection, 175 Milligrams/17.5 Milliliters and 250 Milligrams/25 Milliliters, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness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) has determined that FUSILEV (levoleucovorin calcium), Injection, 175 milligrams (mg)/17.5 milliliters (mL) and 250 mg/25 mL, were not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for levoleucovorin calcium, injection, 175 mg/17.5 mL and 250 mg/25 mL, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: Darren Eicken, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6206, Silver Spring, MD 20993-0002, 240-402-0978.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 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approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (§ 314.162 (21 CFR 314.162)).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may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness.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)). FDA may not approve an ANDA that does not refer to a listed drug.

FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL and 250 mg/25 mL, are the subjects of NDA 020140, held by Spectrum Pharmaceuticals, and were initially approved on April 29, 2011 (supplemental approval). FUSILEV is indicated for rescue after high-dose methotrexate therapy in osteosarcoma, to diminish the toxicity and counteract the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists, and for use in combination chemotherapy with 5-fluorouracil in the palliative treatment of patients with advanced metastatic colorectal cancer.

FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL and 250 mg/25 mL, are currently listed in the "Discontinued Drug Product List" section of the Orange Book. Spectrum Pharmaceuticals has never marketed FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL. In previous instances (see, e.g., 72 FR 9763 and 61 FR 25497), the Agency has determined that, for purposes of §§ 314.161 and 314.162, never marketing an approved drug product is equivalent to withdrawing the drug from sale.

Lachman Consultant Services, Inc. (Lachman), submitted two citizen petitions, dated March 18, 2014, and May 14, 2014 (Docket Nos. FDA-2014-P-0315 and FDA-2014-P-0637, respectively), under 21 CFR 10.30, requesting that the Agency determine whether FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL and 250 mg/25 mL, were withdrawn from sale for reasons of safety or effectiveness.

After considering the Lachman citizen petitions and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL and 250 mg/25 mL, were not withdrawn from sale for reasons of safety or effectiveness. Lachman has identified no data or other information suggesting that FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL and 250 mg/25 mL, were withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal from sale of FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL and 250 mg/25 mL. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have reviewed the available evidence and determined that these products were not withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL and 250 mg/25 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. ANDAs that refer to FUSILEV (levoleucovorin calcium), Injection, 175 mg/17.5 mL and 250 mg/25 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 these drug products should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: August 19, 2014.

Peter Lurie,

Associate Commissioner for Policy and Planning.

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