



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-P-0081]

Determination That CHLOROMYCETIN (Chloramphenicol) Capsules, 250 Milligrams, Were Withdrawn From Sale for Reasons of Safety or Effectiveness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and Drug Administration (FDA) has determined that CHLOROMYCETIN (chloramphenicol) Capsules, 250 milligrams (mg), were withdrawn from sale for reasons of safety or effectiveness. The Agency will not accept or approve abbreviated new drug applications (ANDAs) for chloramphenicol capsules, 250 mg.

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 (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 only clinical data required in an ANDA are data to show that the drug that is the subject of the ANDA is bioequivalent to the listed drug.

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approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).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may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)).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.

CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, are the subject of ANDA 60-591, held by Parkedale Pharmaceuticals, and initially approved on December 8, 1950.

CHLOROMYCETIN is an antibiotic indicated to treat only serious infections for which less potentially dangerous drugs are ineffective or contraindicated.

In a letter dated October 9, 2007, Parkedale Pharmaceuticals requested withdrawal of ANDA 60-591 for CHLOROMYCETIN (chloramphenicol) Capsules, 50 mg, 100 mg and 250 mg. In the Federal Register of February 11, 2009 (74 FR 6896), FDA announced that it was withdrawing approval of ANDA 60-591, effective March 13, 2009, and moved the drug to the “Discontinued Drug Product List” section of the Orange Book.

Armenpharm, Ltd., submitted a citizen petition dated February 7, 2011 (Docket No. FDA-2011-P-0081), under 21 CFR 10.30, requesting that the Agency determine whether CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, were withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petition, and based on the information we have at this time, FDA has determined under § 314.161 that CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, were withdrawn for reasons of safety or effectiveness. We have carefully reviewed Agency records concerning the withdrawal of CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. At the time of the approval of CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, there was significant unmet medical need. With the approval of additional therapies with less severe adverse drug effects, FDA has determined that the risks associated with CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, as currently labeled, outweigh the benefits. Most importantly, CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, may cause a number of adverse reactions, the most serious being bone marrow depression (anemia, thrombocytopenia, and granulocytopenia temporally associated with treatment). A boxed warning in the prescribing information for both chloramphenicol sodium succinate injection and chloramphenicol capsules states that serious hypoplastic anemia,

thrombocytopenia, and granulocytopenia are known to occur after administration of chloramphenicol. The drug product labeling recommends extensive safety monitoring, including baseline blood studies followed by periodic blood studies approximately every 2 days during therapy. The boxed warning also describes fatal aplastic anemia associated with administration of the drug and aplastic anemia attributed to chloramphenicol that later terminated in leukemia. There is published literature which suggests that the risk of fatal aplastic anemia associated with the oral formulation of chloramphenicol may be higher than the risk associated with the intravenous formulation.

FDA has also reviewed the latest approved labeling for the product and has determined that this labeling is inadequate and a Risk Evaluation and Mitigation Strategy (REMS) would be required to ensure that the benefits of the drug outweigh its risks. The REMS may include Elements to Assure Safe Use, including restricted distribution, and a Medication Guide could be required as part of the labeling. FDA has determined that additional nonclinical and possibly clinical studies of safety and efficacy would be necessary before CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, could be considered for reintroduction to the market.

Accordingly, the Agency will remove CHLOROMYCETIN (chloramphenicol) Capsules, 250 mg, from the list of drug products published in the Orange Book. FDA will not accept or approve ANDAs that refer to this drug product.

Dated: July 10, 2012.

Leslie Kux,

Assistant Commissioner for Policy.