4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA-2022-P-2752 and FDA-2022-P-3125]

Determination That Lithium Citrate Oral Solution, 8 Milliequivalents/5 Milliliters, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness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(FDA or Agency) has determined that lithium citrate oral solution, 8 milliequivalents (mEq)/5 milliliters (mL), was not withdrawn from sale for reasons of safety or effectiveness.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 this drug product, and it will allow FDA to continue to approve ANDAs that refer to the product as long as they meet relevant legal and regulatory requirements.

FOR FURTHER INFORMATION CONTACT: Caitlin Callahan, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6240, Silver Spring, MD 20993-0002, 240-402-4318, Caitlin.Callahan@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and (with certain exceptions) labeling as the listed drug, which is a version of the drug that was previously approved and (2) is bioequivalent to the listed drug. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

Section 505(j)(7) of the FD&C Act 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approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).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may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness.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.

Lithium citrate oral solution, 8 mEq/5 mL, is the subject of NDA 018421, held by Hikma Pharmaceuticals USA Inc., and initially approved on December 23, 1980.[1] Lithium citrate oral solution is a mood-stabilizing agent indicated as monotherapy for the following treatment of bipolar I disorder: treatment of acute manic and mixed episodes in patients 7 years and older; and maintenance treatment in patients 7 years and older.

Lithium citrate oral solution, 8 mEq/5 mL, is currently listed in the "Discontinued Drug Product List" section of the Orange Book. Saptalis Pharmaceuticals, LLC submitted a citizen petition dated November 2, 2022 (Docket No. FDA-2022-P-2752), under § 10.30 (21 CFR 10.30), requesting that the Agency determine whether lithium citrate oral solution, 8 mEq/5 mL, was withdrawn from sale for reasons of safety or effectiveness. Hyman, Phelps &

[1] In their citizen petitions, petitioners Saptalis Pharmaceuticals LLC, and Hyman, Phelps & McNamara, P.C., refer to this drug product, respectively, as "Lithium Citrate Syrup EQ 300 mg Carbonate/5mL" and "Lithium Citrate Oral Syrup, 300 mg Carbonate/5mL." The currently approved labeling refers to this drug product as "Lithium Oral Solution USP, 8 mEq per 5 mL" and provides that the dosage strength for Lithium Oral Solution in terms of lithium content, 8 mEq/5mL, is equivalent to 300 mg lithium carbonate/5 mL. For purposes of this determination, we use the current label's description, "Lithium Oral Solution USP, 8 mEq per 5 mL."

McNamara, P.C. separately submitted a citizen petition dated December 6, 2022 (Docket No. FDA-2022-P-3125), under § 10.30, requesting that the Agency make the same determination.

After considering the citizen petitions and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that lithium citrate oral solution, 8 mEq/5 mL, was not withdrawn for reasons of safety or effectiveness. The Petitioners have identified no data or other information suggesting that lithium citrate oral solution, 8 mEq/5 mL, was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of lithium citrate oral solution, 8 mEq/5 mL, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have found no information that would indicate that this drug product was withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list lithium citrate oral solution, 8 mEq/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 to this drug product. Additional ANDAs for this drug product may also 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: March 1, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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