4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-P-3877]

Determination That GLUCOPHAGE (Metformin Hydrochloride) Oral Tablets, 500 Milligrams, 850 Milligrams, and 1 Gram, and GLUCOPHAGE XR (Metformin Hydrochloride) Oral Extended-Release Tablets, 500 Milligrams and 750 Milligrams, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness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, Agency, or we) has determined that, GLUCOPHAGE (metformin hydrochloride) oral tablets, 500 milligrams (mg), 850 mg, and 1 gram (g), and GLUCOPHAGE XR (metformin hydrochloride) oral extended-release tablets, 500 mg and 750 mg, were not withdrawn from sale for reasons of safety or effectiveness.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 these drug products, and it will allow FDA to continue to approve ANDAs that refer to these products as long as they meet relevant legal and regulatory requirements.

FOR FURTHER INFORMATION CONTACT: Carlarease Hunter, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6213, Silver Spring, MD 20993-0002, 301-796-3702, Carlarease.Hunter@fda.hhs.gov.

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.

GLUCOPHAGE (metformin hydrochloride) oral tablets, 500 mg, 850 mg, and 1 g, are the subject of NDA 020357, held by EMD Serono Inc. and initially approved on March 3, 1995. GLUCOPHAGE is indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients 10 years of age and older with type 2 diabetes mellitus.

GLUCOPHAGE (metformin hydrochloride) oral tablets, 500 mg, 850 mg, and 1 g, are currently listed in the "Discontinued Drug Product List" section of the Orange Book.

GLUCOPHAGE XR (metformin hydrochloride) oral extended-release tablets, 500 mg and 750 mg, are the subject of NDA 021202, held by EMD Serono Inc. and initially approved on October 13, 2000. GLUCOPHAGE XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. GLUCOPHAGE XR (metformin hydrochloride) oral extended-release tablets, 500 mg and 750 mg, are currently listed in the "Discontinued Drug Product List" section of the Orange Book.

Harman Finochem Ltd. submitted a citizen petition dated August 17, 2019 (Docket No. FDA-2019-P-3877), under 21 CFR 10.30, requesting that FDA confirm that GLUCOPHAGE (metformin hydrochloride) oral tablets were not withdrawn from sale for reasons of safety or effectiveness. Although the citizen petition did not address the GLUCOPHAGE XR (metformin hydrochloride) oral extended-release tablets, 500 mg and 750 mg, those products have also been discontinued. On our own initiative, we have also determined whether those products were withdrawn for safety or effectiveness reasons.

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 GLUCOPHAGE (metformin hydrochloride) oral tablets, 500 mg, 850 mg, and 1 g, and GLUCOPHAGE XR (metformin hydrochloride) oral extended-release tablets, 500 mg and 750 mg, were not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that GLUCOPHAGE (metformin hydrochloride) oral tablets were withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of GLUCOPHAGE (metformin hydrochloride) oral tablets,

500 mg, 850 mg, and 1 g, and GLUCOPHAGE XR (metformin hydrochloride) oral extended-release tablets, 500 mg and 750 mg, 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 these drug products were not withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list GLUCOPHAGE (metformin hydrochloride) oral tablets, 500 mg, 850 mg, and 1 g, and GLUCOPHAGE XR (metformin hydrochloride) oral extended-release tablets, 500 mg and 750 mg, 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 these drug products. Additional ANDAs for these drug products 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 these drug products should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: December 26, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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