



## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket Nos. FDA-2020-P-1511 and FDA-2020-P-1549]

### Determination That NYMALIZE (nimodipine), Oral Solution, 3 Milligrams/Milliliter, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness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, the Agency, or we) has determined that NYMALIZE (nimodipine), oral solution, 3 milligrams (mg)/milliliter (mL), was not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for nimodipine, oral solution, 3 mg/mL, if all other legal and regulatory requirements are met.

**FOR FURTHER INFORMATION CONTACT:** Ayako Sato, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6206, Silver Spring, MD 20993-0002, 240-402-4191, [Ayako.sato@fda.hhs.gov](mailto:Ayako.sato@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 (FD&C 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.” 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approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162; section 505(j)(7) of the FD&C Act).

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may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness (§ 314.161 (21 CFR 314.161)). 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. FDA may not approve an ANDA that does not refer to a listed drug (see section 505(j)(4) of the FD&C Act).

NYMALIZE (nimodipine), oral solution, 3 mg/mL, is the subject of NDA 203340, held by Arbor Pharmaceuticals, LLC (Arbor), and initially approved on May 10, 2013. NYMALIZE is indicated for the improvement of neurological outcome by reducing the incidence and severity of ischemic deficits in adult patients with subarachnoid hemorrhage from ruptured intracranial berry aneurysms regardless of their post-ictus neurological condition (i.e., Hunt and Hess Grades I through V).

In a letter dated May 4, 2020, Arbor notified FDA that NYMALIZE (nimodipine), oral solution, 3 mg/mL was being discontinued, and FDA moved the drug product to the “Discontinued Drug Product List” section of the Orange Book. As indicated in the Orange Book, Arbor markets a 6 mg/mL strength of NYMALIZE (nimodipine) oral solution, which was approved through NDA 203340/S-011 on April 8, 2020.

Annora Pharma Private Limited submitted a citizen petition dated June 6, 2020 (Docket No. FDA-2020-P-1511) and Windels Marx Lane & Mittendorf, LLC submitted a citizen petition dated June 10, 2020 (Docket No. FDA-2020-P-1549), both under 21 CFR 10.30, requesting that

the Agency determine whether NYMALIZE (nimodipine), oral solution, 3 mg/mL was withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petitions and comments submitted to the dockets and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that NYMALIZE (nimodipine), oral solution, 3 mg/mL, was not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that NYMALIZE (nimodipine), oral solution, 3 mg/mL, was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of NYMALIZE (nimodipine), oral solution, 3 mg/mL, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events.

A comment submitted by Arbor suggests that it was necessary to discontinue marketing the 3 mg/mL strength to mitigate potential confusion between the 3 mg/mL and 6 mg/mL strengths of NYMALIZE (nimodipine), oral solution. FDA disagrees. While discontinuation of the 3 mg/mL strength is one way to reduce the risk of confusion between the two strengths, there are other (often-used) mitigation strategies that may be employed to reduce the risk of confusion among multiple marketed strengths of a drug that could have been used by Arbor. Arbor's comment also states that FDA should find that the 3 mg/mL strength was discontinued for safety reasons because the Agency made similar determinations for BREVIBLOC (esmolol hydrochloride) injection, 250 mg/mL, 10-mL ampule, and the original formulation of PROTONIX I.V. (pantoprazole sodium) for injection. Our finding that the 3 mg/mL strength for NYMALIZE was not withdrawn from sale for reasons of safety is factually distinguishable from BREVIBLOC and PROTONIX I.V.

Based on a thorough evaluation of the information we have available to us and the latest version of the approved labeling for NYMALIZE (nimodipine), oral solution, 3 mg/mL, we have determined that this drug product would be considered safe and effective if it were reintroduced

to the market today. Certain labeling changes should be considered to prevent future medication errors due to the presence of two different strengths of NYMALIZE (nimodipine), oral solution, on the market (i.e., NYMALIZE (nimodipine), oral solution, 3 mg/mL and NYMALIZE (nimodipine), oral solution, 6 mg/mL), but no existing safety signals or efficacy concerns make labeling changes necessary.

Accordingly, the Agency will continue to list NYMALIZE (nimodipine), oral solution, 3 mg/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 NYMALIZE (nimodipine), oral solution, 3 mg/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: February 10, 2021.

**Lauren K. Roth,**

*Acting Principal Associate Commissioner for Policy.*

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