



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-N-1097]

AbbVie Inc.; Withdrawal of Approval of New Drug Applications for ADVICOR and SIMCOR

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is withdrawing approval of the new drug applications (NDAs) for ADVICOR (niacin extended-release (ER) and lovastatin) tablets and SIMCOR (niacin ER and simvastatin) tablets. The holder of these two applications, AbbVie Inc., has requested that FDA withdraw approval of the applications and has waived its opportunity for a hearing. The Agency has also determined that ADVICOR and SIMCOR were withdrawn from sale for reasons of safety and effectiveness, and FDA will not accept or approve abbreviated new drug applications (ANDAs) that reference ADVICOR or SIMCOR.

DATES: The effective date is [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: For access to the docket to read background documents, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management (HFA-305), 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Jay Sitlani, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6282, Silver Spring, MD 20993-0002, 301-796-5202.

SUPPLEMENTARY INFORMATION:

I. Background

FDA approved NDA 021249 for ADVICOR on December 17, 2001. ADVICOR is a fixed-combination drug product containing niacin ER and lovastatin in tablet form. The drug is approved in four strengths of niacin ER and lovastatin, respectively: (1) 500 milligrams (mg), 20 mg; (2) 750 mg, 20 mg; (3) 1 gram (g), 20 mg; and (4) 1 g, 40 mg. The approved indication reads as follows:

ADVICOR is indicated for the treatment of primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Frederickson Types IIa and IIb; Table 6) in:

- Patients treated with lovastatin who require further TG-lowering or HDL-raising who may benefit from having niacin added to their regimen
- Patients treated with niacin who require further LDL-lowering who may benefit from having lovastatin added to their regimen

The indication was revised subsequent to the initial approval and currently states that ADVICOR is approved for the treatment of hypercholesterolemia when treatment with both Niaspan and lovastatin is appropriate.

FDA approved NDA 022078 for SIMCOR on February 15, 2008. SIMCOR is a fixed-combination drug product containing niacin ER and simvastatin in tablet form. The drug is approved in five strengths of niacin ER and simvastatin, respectively: (1) 500 mg, 20 mg; (2) 500 mg, 40 mg; (3) 750 mg, 20 mg; (4) 1 g, 20 mg; and (5) 1 g, 40 mg. SIMCOR is approved for the following indications:

- To reduce TC, LDL-C, apolipoprotein B, non-HDL-C, triglycerides (TG), or to increase HDL-C in patients with primary hypercholesterolemia and mixed

dyslipidemia when treatment with simvastatin monotherapy or niacin ER monotherapy is considered inadequate

- To reduce TG in patients with hypertriglyceridemia when treatment with simvastatin monotherapy or niacin ER monotherapy is considered inadequate

The labeling includes the following Limitation of Use in the Indications and Usage section of the labeling:

- No incremental benefit of SIMCOR on cardiovascular morbidity and mortality over and above that demonstrated for simvastatin monotherapy and niacin monotherapy has been established.

II. Withdrawal Under Section 505(e) of the FD&C Act

Based on the collective evidence from several large cardiovascular outcome trials (Refs. 1-3.), the Agency has concluded that the totality of the scientific evidence no longer supports the conclusion that a drug-induced reduction in triglyceride levels and/or increase in HDL-cholesterol levels in statin-treated patients results in a reduction in the risk of cardiovascular events. Consistent with this conclusion, FDA has determined that the benefits of ADVICOR and SIMCOR no longer outweigh the risks, and approval should be withdrawn.

FDA requested that AbbVie Inc. voluntarily discontinue marketing of ADVICOR and SIMCOR, and AbbVie Inc. agreed to do so. AbbVie Inc. also has requested in writing that FDA withdraw approval of NDA 021249 and NDA 022078 and waived its opportunity for a hearing.

Therefore, under section 505(e) of the FD&C Act and under authority delegated to the Director of the Center for Drug Evaluation and Research by the Commissioner of Food and Drugs, approval of ADVICOR and SIMCOR is withdrawn. Introduction or delivery for

introduction of these products without an approved application is illegal and subject to regulatory action (see sections 505(a) and 301(d) of the FD&C Act (21 U.S.C. 355(a) and 331(d)).

The Agency is required to publish a list of all approved drugs (see section 505(j)(7) of the FD&C Act (21 U.S.C. 355(j)(7)). 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 314.161 and 314.162(a)(2)). For the reasons summarized in this document, the Agency has determined that ADVICOR and SIMCOR were voluntarily withdrawn from sale for reasons of safety or effectiveness. FDA will remove NDA 021249 for ADVICOR and NDA 022078 for SIMCOR from the list of products published in the Orange Book and will not accept or approve ANDAs that reference either drug product.

III. References

The following references are on display in the Division of Dockets Management (see ADDRESSES), and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at <http://www.regulations.gov>. FDA has verified the Web site addresses, as of the date this document publishes in the Federal Register, but Web sites are subject to change over time.

1. The ACCORD Study Group, “Effects of Combination Lipid Therapy in Type 2 Diabetes Mellitus,” New England Journal of Medicine, vol. 362, pp. 1563-1574, 2010 (<http://www.nejm.org/doi/pdf/10.1056/NEJMoa1001282>).

2. The AIM-HIGH Investigators, “Niacin in Patients with Low HDL Cholesterol Levels Receiving Intensive Statin Therapy,” New England Journal of Medicine, vol. 365, pp. 2255-2267, 2011 (<http://www.nejm.org/doi/pdf/10.1056/NEJMoa1107579>).
3. The HPS2-THRIVE Collaborative Group, “Effects of Extended-Release Niacin with Laropiprant in High-Risk Patients,” New England Journal of Medicine, vol. 371(3), pp. 203-212, 2014 (<http://www.nejm.org/doi/pdf/10.1056/NEJMoa1300955>).

Dated: April 13, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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