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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 316

[Docket No. FDA-2011-N-0583]

Policy on Orphan-Drug Exclusivity; Clarification

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification; clarification on policy.

SUMMARY: The Food and Drug Administration (FDA) is publishing this document to clarify its policy regarding certain aspects of orphan-drug exclusivity. This document is being published because of a recent court decision interpreting provisions of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Orphan Drug Act.

DATES: Effective December 23, 2014.

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SUPPLEMENTARY INFORMATION:

I. Background

After a designated orphan drug is approved, section 527 of the FD&C Act (21 U.S.C. 360cc) generally prohibits the Food and Drug Administration (FDA or the Agency) from approving another such drug for the same disease for 7 years. Regulations interpreting this provision were proposed in 1991 (January 29, 1991, 56 FR 3338) and made final in 1992 (December 29, 1992, 57 FR 62076). In 2011, FDA issued a proposed rule (October 19, 2011, 76

FR 64868) to amend these regulations to clarify certain regulatory language and propose areas of minor improvement regarding orphan-drug designation and orphan-drug exclusivity; these were finalized in 2013 (June 12, 2013, 78 FR 35117). These regulations are codified under part 316 (21 CFR Part 316).

FDA has interpreted section 527 of the FD&C Act and its regulations such that the Agency will not recognize orphan-drug exclusivity for a drug when it has previously approved the same drug for the same use or indication in a rare disease or condition. §§ 316.3(b)(12); 316.31(a). A drug will not be considered the same as a previously approved drug if, at the time of approval, the sponsor has provided evidence that its drug is "clinically superior" to the previously approved drug, that is, the drug is more effective, safer, or makes a major contribution to patient care. § 316.3(b)(3). Accordingly, the sponsor of an orphan-designated drug that is the same as a previously approved drug, as defined in § 316.3(b)(14), is required to demonstrate that its drug is clinically superior to the previously approved drug in order for its drug to be eligible for orphan-drug exclusivity upon approval.

The Agency's interpretation of section 527 of the FD&C Act has been the subject of legal action in Depomed v. HHS et al., Civil Action No. 12-1592 (KBJ) (D.D.C. September 5, 2014). Depomed has not demonstrated that GRALISE (gabapentin) is clinically superior to a previously approved drug, Pfizer's NEURONTIN (gabapentin). Accordingly, under the relevant regulations, GRALISE is the same drug as NEURONTIN, because it contains the same active moiety (gabapentin), was approved for the same use (post-herpetic neuralgia), and was not demonstrated to be clinically superior to NEURONTIN. Nevertheless, the Depomed court held that FDA must recognize orphan-drug exclusivity for GRALISE for the treatment of post-

herpetic neuralgia. Following the Depomed decision, under the court's order, FDA recognized orphan-drug exclusivity for GRALISE for the treatment of post-herpetic neuralgia.

II. Orphan-Drug Exclusivity

In consideration of any uncertainty created by the court's decision in Depomed, the Agency is issuing this statement. It is the Agency's position that, given the limited terms of the court's decision to GRALISE, FDA intends to continue to apply its existing regulations in part 316 to orphan-drug exclusivity matters. FDA interprets section 527 of the FD&C Act and its regulations (both the older regulations that still apply to original requests for designation made on or before August 12, 2013, as well as the current regulations) to require the sponsor of a designated drug that is the "same" as a previously approved drug to demonstrate that its drug is "clinically superior" to that drug upon approval in order for the subsequently approved drug to be eligible for orphan-drug exclusivity.

Dated: December 17, 2014.

Leslie Kux,

Associate Commissioner for Policy.

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