



**Interpretive Rule: Implementation of the Exclusion of Orphan Drugs for
Certain Covered Entities Under the 340B Program**

HHS is issuing this interpretive rule to set forth HHS’s interpretation of section 340B(e) of the Public Health Service Act (PHSA), “Exclusion of Orphan Drugs for Certain Covered Entities.” For the affected entities within its scope, HHS interprets section 340B(e) of the PHSA as excluding from the 340B Drug Pricing Program (“340B Program”) drugs that are transferred, prescribed, sold, or otherwise used for the rare condition or disease for which the drug was designated under section 526 of the Federal Food, Drug, and Cosmetic Act (FFDCA). However, section 340B(e) of the PHSA does not exclude from the 340B Program drugs that are transferred, prescribed, sold, or otherwise used for conditions or diseases other than for which the drug was designated under section 526 of the FFDCA. The purpose of this document is to describe the manner in which section 340B(e) of the PHSA will be interpreted and implemented by HHS. The effective date is July 21, 2014. For further information, please contact CDR Krista Pedley, Director, Office of Pharmacy Affairs, Healthcare Systems Bureau, HRSA, 5600 Fishers Lane, Room 8W03A, Rockville, MD 20857, or by telephone at (301) 594-4353.

I. Background

A. The 340B Program

The 340B Program was established by section 602 of the Veterans Health Care Act of 1992 (Pub. L. 102-585), which added section 340B to the PHSA. Section 340B instructs HHS to enter into agreements with drug manufacturers of covered outpatient drugs. 42 U.S.C. 256b(a).

The purpose of the 340B Program is to permit covered entities “to stretch scarce Federal resources as far as possible, reaching more eligible patients and providing more comprehensive services.” H.R. Rep. No.102–384(II), at 12 (1992). Pursuant to section 340B(a)(1) of the PHSA, when a manufacturer signs a Pharmaceutical Pricing Agreement (PPA), it agrees that the prices charged for covered outpatient drugs to covered entities (organizations eligible under section 340B to receive 340B discounted pricing) will not exceed defined ceiling prices, which are based on pricing data reported to the Centers for Medicare & Medicaid Services (CMS). Drugs purchased by covered entities through the 340B Program may not be sold or transferred to anyone other than the patients of the covered entities.

The Patient Protection and Affordable Care Act (“Affordable Care Act”) (Public Law 111-148) and the Health Care and Education Reconciliation Act (HCERA) (Public Law 111-152) made several changes to the 340B Program. Section 7101 of the Affordable Care Act added several new categories of eligibility for 340B Program participants, allowing them to have access to 340B drug pricing. The entity types added to the list of eligible entities listed under 340B(a)(4) included: 340B(a)(4)(M) (children's hospitals and free-standing cancer hospitals), 340B(a)(4)(N) (critical access hospitals), and 340B(a)(4)(O) (rural referral centers and sole community hospitals). It also excluded free-standing cancer hospitals, critical access hospitals, rural referral centers, and sole community hospitals from access to 340B drug pricing for a drug when it is used for a rare disease or condition. As amended by HCERA and section 204 of the Medicare and Medicaid Extenders Act of 2010 (Public Law 111-309), section 340B(e) of the PHSA (42 U.S.C. 256b(e)) states the following:

EXCLUSION OF ORPHAN DRUGS FOR CERTAIN COVERED ENTITIES—For covered entities described in subparagraph (M) (other than a children's hospital described in subparagraph (M)), (N), or (O) of subsection (a)(4), the term ‘covered outpatient drug’ shall not include a drug designated by the Secretary under section 526 of the Federal

Food, Drug, and Cosmetic Act for a rare disease or condition.

After notice and comment rulemaking, HRSA issued a final rule on this subject, “Exclusion of Orphan Drugs for Certain Covered Entities Under 340B Program” (78 FR 44016, July 23, 2013) (the “Rule”). The Rule was vacated by U.S. District Court for the District of Columbia on May 23, 2014, on the grounds that HHS does not have the authority to issue the Rule as a substantive rule. *PhRMA v. HHS*, No. 13-01501 (D.D.C. May 23, 2014). However, the decision did not invalidate HHS’s interpretation of the orphan drug exclusion in the Rule.

B. The Orphan Drug Act

Congress passed the Orphan Drug Act of 1983 to stimulate the development of drugs for rare diseases. The Food and Drug Administration (FDA) administers the Orphan Drug Act and reviews requests for designations. A drug is designated by the FDA as “a drug for a rare disease or condition” pursuant to section 526 of the FDCA at the request of the sponsor if FDA finds that the drug is being or will be investigated for a rare disease or condition and, if approved by FDA, the approval will be for that disease or condition. 21 U.S.C. 360bb(a)(1). This designation is referred to as orphan-drug designation. 21 CFR 316.24. The orphan drug designation may provide a number of incentives for the development of the orphan drug for the particular disease or condition. These incentives, described in more detail below, may include: (1) 7-year market exclusivity; (2) a tax credit of 50 percent of the cost of conducting qualified human clinical trials; and (3) an exemption from the usual drug application “user” fees charged by the FDA; 21 U.S.C. 360cc; 26 U.S.C. 45C; 21 U.S.C. 379h(a)(1)(F).

FDA will designate a drug for a rare disease or condition as an orphan drug in situations even if the drug is also approved for a different disease or condition that does not qualify for such a designation. 21 CFR 316.23(b). However, each of the incentives applies only to the

orphan drug indication – that is to the use of the drug intended to treat the rare disease or condition and not to other (non-orphan) indications, as described below.

First, the marketing exclusivity only applies to the use of the drug that has been approved by FDA to treat an orphan rare disease or condition. Thus, only applications for drugs intended to be used to treat the orphan disease or condition are blocked. If the same drug has been approved by FDA for one or more non-rare uses, the orphan drug market exclusivity provides no market protection. Second, the tax credit must relate to testing of the drug for the rare disease or condition underlying the orphan designation and not for the testing for other diseases or conditions (non-rare uses). Finally, the exemption from FDA user fee payments only applies to user fees charged when seeking marketing approval for the use to treat the orphan designated rare disease or condition. The exemption does not apply to user fees charged for applications that seek marketing approval for non-rare uses as well as a rare disease or condition. None of the incentives associated with orphan drug designation applies to any indication for a disease or condition that is not rare. For those non-rare disease or condition indications, the drug would not be considered to be an “orphan drug.”

C. Construing the 340B Exclusion of Orphan Drugs for Certain Covered Entities

The exclusion in section 340B(e) specifically references the designation of drugs for a rare disease or condition under the FFDCA. FDA is the agency statutorily designated to execute the FFDCA, including the orphan drug provisions. 21 U.S.C. 393(d)(2). Therefore, it is appropriate to construe the orphan drug exclusion consistent with FDA’s longstanding interpretation of the orphan drug provisions of the FFDCA—distinguishing the use of a drug for an orphan indication from its use for other (non-orphan) indications. The fact that drugs can have multiple indications, only some of which qualify for orphan designation, has led HHS to

conclude that the exclusion from the term “covered outpatient drug” under section 340B(e) of the PHSA only applies to drugs when they are transferred, prescribed, sold, or otherwise used for the rare condition or disease for which the drug was designated.

This interpretation is consistent with the language of the exclusion in 340B(e) of the PHSA, which states that it applies to drugs “for a rare disease or condition.” As previously mentioned, the Affordable Care Act added four newly-eligible covered entity categories to benefit from the 340B Program. As Congress wanted these new covered entities to participate and benefit from the 340B Program “to stretch scarce federal resources as far as possible, reaching more eligible patients and providing more comprehensive services,” it is critical that HHS recognizes these covered entities’ ability to benefit from the 340B Program savings so there is sufficient value for them to participate in the 340B Program. HHS has been notified by covered entities that some of the newly-eligible covered entities are significant purchasers of drugs with an orphan designation, and if these drugs were excluded from the 340B Program entirely, it is not clear if there would be sufficient financial benefits to participate. Interpreting the statutory language to exclude all uses of drugs with an orphan designation, including indications for other (non-orphan) diseases and conditions, would nullify the benefits of the expansion of the 340B Program for these entities. Therefore, we have concluded that interpreting the statutory language to exclude all indications for a drug that has an orphan drug designation would be contrary to the Congressional intent of section 340B(e) to balance the interests of orphan drug development and the expansion of the 340B Program to new entities.

Designations under section 526 of the FFDCA are the responsibility of and administered by the FDA. FDA publishes information pertaining to orphan drug designations pursuant to 21 CFR part 316. To facilitate identification of drugs with an orphan designation for 340B Program

purposes, HRSA will publish a listing of orphan drug designations, providing the name of the drug and the designated indication. The list will be published on the first day of the month prior to the end of the calendar quarter. If a covered entity lacks the ability to track drug use by indication, such entity would be unable to purchase drugs with orphan designations through the 340B Program. Updated on a quarterly basis, HRSA will maintain a list of covered entities that cannot or do not wish to purchase such drugs through the 340B Program.

Section 340B(a)(4)(L)(iii) of the PHSA requires certain hospitals participating in the 340B Program to “not obtain covered outpatient drugs through a group purchasing organization or other group purchasing arrangement.” The 340B statute prevents disproportionate share hospitals, children's hospitals, and free-standing cancer hospitals from obtaining covered outpatient drugs through a group purchasing organization (GPO). Of those entities, only free-standing cancer hospitals are impacted by the orphan drug exclusion. HHS interprets this GPO prohibition as not applying to purchases of drugs when they are transferred, prescribed, sold, or otherwise used for the rare condition or disease for which that drug was designated under section 526 of the FFDCA, as these drugs are not covered outpatient drugs for purposes of the 340B Program. However, this GPO prohibition does apply to purchases of drugs when they are transferred, prescribed, sold, or otherwise used for conditions or diseases other than for which that drug was designated under section 526 of the FFDCA.

II. Interpretive Rule

HHS interprets section 340B(e) of the Public Health Service Act as excluding drugs with an orphan designation only when those drugs are transferred, prescribed, sold, or otherwise used for the rare condition or disease for which the drug was designated under section 526 of the Federal Food, Drug, and Cosmetic Act (FFDCA). Section 340B(e) does not exclude drugs that

are transferred, prescribed, sold, or otherwise used for conditions or diseases other than for which the drug was designated under section 526 of the FDCA.