HRSA Issues Proposed Rule on Exclusion of Orphan Drugs for Certain Covered Entities Under the 340B Program

On May 20, 2011, the Health Resources and Services Administration (HRSA) published a proposed rule regarding the exclusion of orphan drugs for certain covered entities under the 340B program.[1] According to HRSA, the proposed rule is the first in a series of regulations that will outline certain requirements of the 340B law, as modified by the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act (together, PPACA). As discussed below, the proposed rule would interpret the 340B orphan drug exemption to apply only where a drug is used for a rare disease or condition for which the drug received orphan designation. The proposed rule does not specify how the covered entity (or the manufacturer) would know, at the time the drug is sold to the covered entity, whether it ultimately will be used for an orphan indication. The proposed rule would also allow certain covered entities to use a group purchasing organization (GPO) to purchase orphan drugs used for orphan indications.

I. Overview of the Proposed Rule

Among other things, PPACA amended the 340B law to add several new categories of entities to the 340B program, including certain cancer hospitals, critical access hospitals, rural referral centers, and sole community hospitals.[2] In response to concerns that this expansion in covered entities could reduce incentives for manufacturers to develop and market orphan drugs and therefore undermine the Orphan Drug Act,[3] Congress added an orphan drug exemption to the 340B law. This provision carves out an exemption from 340B discounting obligations with respect to this subset of newly eligible 340B entities. As

1 76 Fed. Reg. 29,183 (Mar. 20, 2011), *available at:* http://www.gpo.gov/fdsys/pkg/FR-2011-05-20/pdf/2011-12423.pdf.

2 42 U.S.C. § 256b(a)(4)(M), (N), and (O). PPACA also added certain children's hospitals to the list of eligible entities in the 340B law. Prior to PPACA, however, the Deficit Reduction Act of 2005 had amended the Medicaid rebate statute to make a similar but somewhat broader group of children's hospitals eligible for 340B prices.

3 21 U.S.C. §§ 360aa *et seq.* (Federal Food, Drug, and Cosmetic Act §§ 525 *et seq.*).

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recently amended by the Medicare and Medicaid Extenders Act of 2010, the exemption provides:

> 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) [of 42 U.S.C. § 256b(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.[4]

HRSA states that this language has generated considerable confusion in the industry regarding: (1) whether this subset of newly eligible covered entities may never purchase orphan drugs through the 340B Program, or whether the language only prohibits purchase of orphan drugs under 340B when the drug will be used for an orphan indication; (2) whether selling orphan drugs through the 340B program to the newly eligible entities could create best price implications; (3) whether these covered entities can purchase orphan drugs using GPOs; and (4) what systems need to be in place to ensure compliance with the exemption.

A. Proposed Application to Orphan Indications Only

The proposed rule would construe the orphan drug exemption to prohibit newly eligible covered entities from purchasing an orphan drug through the 340B program **only** where such drug is "transferred, prescribed, sold, or otherwise used for the rare condition or disease for which that orphan drug was designated under section 526 of the [Federal Food Drug and Cosmetic Act (FFDCA)]."[5] Manufacturers and covered entities seeking to determine whether a drug is designated under section 526 of the FFDCA and the indication(s) for which it is designated would be required to consult the FDA listing of orphan drugs under section 526.[6] In addition, the proposed rule would clarify that the orphan drug exemption does not apply to entities that could potentially qualify as one of the subsets of covered entities to which the exemption would apply (i.e., cancer hospitals, critical access hospitals, rural referral centers, or sole community hospitals), but that are enrolled under a different category of covered entity. For example, as HRSA explained, "if a hospital potentially qualifies both under 340B(a)(4)(L) as a disproportionate share hospital and under 340B(a)(4)(O) as a sole community hospital, then that hospital must select which type and enroll under the requirements of the type that is selected."[7]

In explaining its interpretation of the orphan drug exemption, HRSA does not directly address the plain language of the provision, which creates an exemption for "a drug" designated by the Secretary as a drug for a rare disease or condition (irrespective of whether the designated drug may have non-orphan indications, or may be used for a non-orphan indication by a 340B entity). By its terms, the exemption covers any drug designated for a rare disease or condition; there is no extra requirement that the drug be limited to use for the rare disease or condition that allowed its designation, or that the 340B entity use the drug for the rare disease or condition underlying its designation. HRSA's interpretation seems difficult to square with the fundamental principle of statutory construction that statutes must be interpreted in accordance with their plain language.

The proposed rule also does not clearly state whether an orphan designated indication would also have to be approved in order to be eligible for the exemption. However, certain statements in the preamble suggest that the exemption would apply to any designated indication. For example, HRSA reasons that limiting the exemption to orphan indications is consistent with the incentives associated with orphan designation (such as seven years market exclusivity, a clinical trial tax credit, federal research grants for clinical testing, and exemption from the drug application user fee), because these incentives do not apply to any indication that has not itself received orphan drug

4 42 U.S.C. § 256b(e). The recent revision made by the Medicare and Medicaid Extenders Act of 2010, Pub. L. 111-309, § 204, removed children's hospitals described in 42 U.S.C. § 256b(a)(4)(M) from the scope of the orphan drug exemption, because a similar group of children's hospitals had been eligible for 340B pricing before PPACA.

5 76 Fed. Reg. at 29,189 (proposed 42 C.F.R. § 10.21(a)).

6 The FDA listing of orphan drugs is *available at:* http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm.

7 76 Fed. Reg. at 29,186.

designation.[8] Some of these incentives—the clinical trial tax credit and federal research grants for clinical testing—by their nature only apply to orphan designated indications that have not yet been approved. Therefore, the comparison suggests that the exemption would also apply to orphan designated indications that have not yet been approved. Moreover, the economic impact statement of the proposed rule states that "[t]here are approximately 350 drugs that have been approved for rare diseases and conditions…[and] there are another 100 orphan designated drugs that have not been approved for the rare disease but are approved for a common disease….[M]anufacturers of these orphan designated drugs with at least one marketing approval will be affected by this rule."[9] While not explicit, this statement seems to contemplate that drugs with non-approved orphan designations would be affected by the exemption.

B. Potential Best Price Implications—Reasonable Assumptions

Although HRSA acknowledges in the preamble that "some manufacturers have ceased selling orphan drugs through the 340B Program to the newly-eligible covered entities to avoid best price implications,"[10] the proposed rule does not squarely address these concerns. The proposed rule would not resolve the potential best price questions that could result when a manufacturer sells an orphan drug to a covered entity at the 340B ceiling price, and the covered entity ultimately dispenses the drug for a non-orphan indication. Instead, the preamble provides that the Centers for Medicare and Medicaid Services (CMS) "is delegated the responsibility for regulating the Medicaid best price exemption, and HRSA is working with CMS to develop policy on the treatment of orphan drugs…with respect to Medicaid best price."[11] Until CMS issues this policy, however, "manufacturers are permitted to make reasonable assumptions regarding the Medicaid best price calculations, including exclusions applicable to those calculations."[12]

8 *Id.* at 29,184.
9 *Id.* at 29,188.
10 *Id.* at 29,184.
11 *Id.* at 29,185.
12 *Id.*

C. Application of the GPO Prohibition to Orphan Drugs

The proposed rule also addresses the interaction between the orphan drug exemption and the "GPO prohibition," which prohibits certain categories of covered entities from purchasing any covered outpatient drug through a GPO.[13] Among the subset of newly eligible covered entities to which the orphan drug exemption applies, only free-standing cancer hospitals are subject to the GPO prohibition.[14] The proposed rule reiterates the requirement that such entities comply with the GPO prohibition, but provides that "[i]f auditable records are maintained that demonstrate full compliance with orphan drug purchasing requirements, then free-standing cancer hospitals enrolled under 340B(a)(4)(M) are permitted to use a [GPO] to purchase orphan drugs when they are transferred, prescribed, sold, or otherwise used for the rare condition or disease for which that orphan drug was designated under section 526 of the FFDCA, as these drugs are not considered covered outpatient drugs."[15]

Moreover, "[t]o the extent that a free-standing cancer hospital elects to purchase all orphan drugs outside of the 340B program, covered entities are permitted to use a [GPO] for those purchases."[16] Under HRSA's interpretation of the orphan drug exemption, this would allow a covered entity to purchase certain covered outpatient drugs (i.e., orphan drugs used for non-orphan indications) through a GPO, thus raising questions about compliance with the language of the GPO prohibition (which requires that the entity "not obtain covered outpatient drugs through a group purchasing organization or other group purchasing arrangement").[17]

D. Covered Entity Compliance Requirements

While the preamble to the proposed rule acknowledges that "covered entities do not know…if there are additional record-keeping requirements that they must meet for 340B compliance" and "[o]ther 340B stakeholders such as wholesalers are also not sure which systems need to

13 42 U.S.C. § 256b(a)(4)(L)(iii).
14 *See id.* § 256b(a)(4)(M).
15 76 Fed. Reg. at 29,190 (proposed 42 C.F.R. §10.21(d)).
16 *Id.*
17 42 U.S.C. § 256b(a)(4)(L)(iii).

be in place to ensure compliance with this new statutory provision," the proposed covered entity compliance requirements lack specificity.[18] The proposed rule would require covered entities to "maintain separate purchasing accounts and to provide auditable records upon the written request of the government or government-approved manufacturer audit request that directly pertain to the covered entity's compliance with this requirement."[19] The preamble states that "covered entities shall put in place tracking and record-keeping requirements to demonstrate compliance with the limits on the use of orphan drugs. To demonstrate compliance, it will be necessary for the covered entities to create separate purchasing accounts and improve inventory and auditing capacity."[20] The preamble further provides that entities violating the orphan drug exemption shall be subject to the sanctions and penalties applicable to failure to comply with the prohibition on diversion of covered outpatient drugs in section 340B(a)(5)(B).[21] Affected covered entities that cannot or do not wish to maintain auditable records sufficient to demonstrate compliance may purchase all orphan drugs outside of the 340B program, and must notify HRSA of this when they enroll in the program and during recertification.

II. Practical Challenges

HRSA's proposal to limit the orphan drug exemption to drugs ultimately used for their orphan indication raises administrative challenges for both manufacturers and covered entities. Whether an orphan drug was a 340B drug (and hence the correct price) would be unknown at the time of sale, as neither the manufacturer nor the covered entity could know what indication the drug would be used for at the time of sale. Similarly, it is unclear how free-standing cancer hospitals would determine that a drug would be used for an orphan indication prior to purchasing that drug through a GPO. The proposed rule does not provide a mechanism for addressing these challenges, but instead only provides that "[m]anufacturers cannot condition sales upon receiving prior assurances that the 340B drug will not be used to treat a rare disease or condition."[22]

Thus, the proposed rule leaves many questions regarding the implementation of the orphan drug exemption unanswered. Prior to the close of the comment period on July 19, 2011, 340B stakeholders may wish to submit comments highlighting the operational challenges and areas of uncertainty resulting from the proposed rule, or asking HRSA to rethink its fundamental approach and take a closer look at the plain language of the orphan drug exemption.

We hope that you have found this advisory useful. If you have questions about the topics discussed in this advisory, please contact your Arnold & Porter attorney or any of the following attorneys:

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18 76 Fed. Reg. at 29,184.

19 *Id.* at 29,189 (proposed 42 C.F.R. § 10.21(c)).

20 *Id.* at 29,186.

21 *Id.*

22 *Id.* at 29,185.