KING & SPALDING

Client Alert

FDA & Life Sciences Practice Group

July 31, 2013

HRSA Issues Final 340B Orphan Drug Exclusion Rule

Agency's Narrow Interpretation of Statutory Prohibition Puts Compliance Responsibility in the Hands of Covered Entities

On July 23, 2013, the Health Resources and Services Administration (HRSA) issued a final rule clarifying the orphan drug exclusion for certain covered entities created by the Affordable Care Act (ACA) ("Final Rule"). The Final Rule is available **here**, has an effective date of **October 1, 2013**, and applies prospectively from that date. The text of the new 340B regulations created by the Final Rule, 42 C.F.R. Part 10, appears at the end of this Client Alert.

In short, the Final Rule permits the new categories of covered entities access to 340B pricing for orphan drugs based on the covered entity's intended use. In one sense, the Agency rule is surprising given statutory language that would appear to limit these covered entities' access to the 340B program's deeply discounted pricing for orphan drugs without regard to the condition the drug will be used to treat. Treatment-specific considerations have never been part of access to 340B discounts: HRSA's new interpretation of the 340B statute is a watershed moment in the history of the 340B Program. Further, HRSA has crafted a rule that puts determination of eligibility to purchase orphan drugs at 340B prices squarely in the hands of the affected covered entities. Drug manufacturers are not afforded any opportunity at the point-of-purchase to gauge the validity of the claim for discounts, and are given little authority after the fact to check the covered entity records that are the sole mechanism of ensuring compliance with the orphan drug exclusion rule, short of audit or referral to HRSA for investigation.

Background

ACA Section 7101 created a statutory exception to the definition of "covered outpatient drug" for free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals participating in the 340B drug discount program. 42 U.S.C. § 256b(e) (also known as Section 340B(e)). The law held that the term, "covered outpatient drug," for those purchasers (the "orphan drug exclusion entities"), does not include "drug[s] designated by the Secretary [of HHS] under section 526 of the Federal Food, Drug, and Cosmetic Act for a rare disease or condition." The Final Rule issued last week is HRSA's interpretation of ACA Section 7101 and guidelines for implementation.

For more information, contact:

John D. Shakow
+1 202 626 5523
jshakow@kslaw.com

Elizabeth F. Gluck
+1 202 626 5585
egluck@kslaw.com

King & Spalding
Washington, D.C.
1700 Pennsylvania Avenue, NW
Washington, D.C. 20006-4707
Tel: +1 202 737 0500
Fax: +1 202 626 3737
www.kslaw.com

In May, 2011, HRSA published its Proposed Rule interpreting the orphan drug exclusion (*see* 76 Fed. Reg. 29,183 (May 20, 2011)). HRSA received over 50 comment letters from Members of Congress, manufacturers, 340B covered entities, providers, and other 340B Program stakeholders. The conclusions of the Final Rule are largely unchanged from those proposed over two years ago.

While HRSA has issued program guidance materials in the past, the Final Rule, codified at 42 C.F.R. Part 10, is the first 340B Program *regulation* issued by HRSA. HRSA indicated in the Final Rule that additional 340B Program regulations would published and be incorporated into this Part in the near future. HRSA personnel indicated at a recent conference that "omnibus" 340B program regulations are being drafted; presumably they would be made part of the new 42 C.F.R. Part 10.

The Final Rule Interpretation of the Orphan Drug Exclusion

The Final Rule holds that under Section 340B(e), the orphan drug exclusion entities are not entitled to purchase orphan-designated drugs at the 340B ceiling price *when such drugs are used for an orphan indication.*[1] The Rule requires manufacturers, however, to extend the 340B ceiling price to these entities when an orphan drug is to be used for an indication *other* than the orphan indication. Specifically, the Final Rule held that Section 340B(e) apples only to "drugs transferred, prescribed, sold, or otherwise used for the rare condition or disease for which the orphan drug was designated under section 526 of FDCA." HRSA will publish a list every quarter of NDCs subject to this analysis, drawn from FDA records.[2]

Many manufacturers had argued that the plain text of Section 340B(e) does not permit an indication-specific interpretation, that the exception to "covered outpatient drug" was *drug*- and not *indication*-specific. If a drug were designated by FDA for any orphan purpose, the commenters urged, the manufacturer of that drug should not be obliged to sell it to the orphan drug exclusion entities at the 340B discount for any use. HRSA disagreed, concluding that to give meaning to the expansion of the 340B program to these entities, orphan-indicated products must be made available at 340B prices when used for other than an orphan indication (to find otherwise would "nullify the benefits of the expansion" of the Program). HRSA concludes that Congress intended to balance the interests of orphan drug research and the expansion of the 340B program to new entities by limiting the orphan drug exclusion to certain indicated uses (despite the lack of statutory language evidencing this position). The Final Rule goes to great lengths to defend this proposition.

---

[1] Manufacturers *may* offer orphan drugs to orphan drug exclusion entities at or below the 340B ceiling price if they so desire. Consistent with 42 U.S.C. § 1396r-8(c)(1)(C)(i)(I), any sales to covered entities for outpatient use at any price are excluded from Best Price. Note, however, that in the ACA AMP Proposed Rule, CMS proposed to include by regulation sales "outside the 340B Program" in Best Price despite the statutory language that would seem to bar such a rulemaking.

[2] For the purposes of the 340B Program, orphan drugs will be identified with reference to the U.S. Food and Drug Administration's orphan drug database. HRSA will maintain a list of these orphan drugs on its 340B Program website. This list will be updated on a quarterly basis, and posted on the first day of the month prior to the end of the calendar quarter to govern purchases made in the following quarter.

The Final Rule specifies that it is the responsibility of the orphan drug exclusion entities to ensure that orphan drugs purchased through the 340B Program "are not transferred, prescribed, sold, or otherwise used for" an orphan-indicated use. To this end, covered entities are required to maintain auditable records and provide them to HRSA upon request, and in connection with government-approved manufacturer audit requests that directly pertain to the covered entities' compliance with Section 340B(e). These auditable records are the only indicators of covered entity compliance required by the Final Rule. Moreover, all contract pharmacies are required under the Final Rule to follow the same approach used by the related covered entity to ensure compliance with the orphan drug exclusion, including implementing the necessary systems and recordkeeping requirements.

The approach outlined in the Final Rule essentially requires drug manufacturers to trust that orphan drug exclusion entities (and their contract pharmacies) will know, at the time a drug is purchased from the wholesaler, to what use that particular unit will one day be put. This information is critical in determining at what price the sale can be made, off of what contract, under what purchaser identification number. Short of maintaining fully segregated inventories or tracking discounted drug through the purchasing and dispensing process, HRSA proposes no specific strategy for covered entity compliance with 340B(e). Alternative tracking systems must be considered and approved by HRSA on a case-by-case basis.

Under new 340B regulation §10.21(s), if a covered entity is unwilling or unable to maintain auditable records establishing compliance with 340B(e), it must purchase all orphan drugs outside of the 340B Program, regardless of the indication for which the drug is to be used. A hospital enrolled in the 340B Program may change its decision whether or not to purchase all orphan drugs outside of the 340B Program on a quarterly basis by notifying HRSA. This documentation will be public and verified during the annual recertification process.

Covered Entities with Dual Qualifications

If a covered entity qualifies as both an entity that is subject to the orphan drug exclusion and an entity that is not (*e.g.*, a disproportionate share hospital and a sole community hospital), the hospital must select which enrollment type it chooses to qualify under and comply with the applicable regulatory and other 340B Program requirements. As part of the registration and annual recertification processes, a covered entity is required to certify that it meets the requirements for its particular enrollment type, including the orphan drug exclusion.

GPO Prohibition and the Orphan Exclusion

Section 10.21(d) clarifies that free-standing cancer hospitals (to which the GPO prohibition applies) are still prohibited from using a GPO for covered outpatient drugs. As orphan drugs when used for an orphan indication are *not* covered outpatient drugs, however, free-standing cancer hospitals may utilize a GPO to purchase these drugs. As the other orphan drug exclusion entities are not subject to the GPO prohibition, they may purchase orphan drugs through GPO arrangements no matter their intended use.

"Must Offer"

Manufacturers submitted comments challenging HRSA's position in the Proposed Rule that manufacturers must extend the 340B ceiling price on an orphan drug if an orphan drug exclusion entity requests it, based on the assumption that the

covered entity would only use the product for a non-orphan indication. Specifically, manufacturers argued that the "must offer" provision of the amended PHS Act (42 U.S.C. § 256b(a)(1)) could not be implemented until HRSA revises its Pharmaceutical Pricing Agreement and manufacturers execute that revised agreement. In the Final Rule, citing a Federal Register notice from 1994 and the Supreme Court's opinion in the *Santa Clara* case, HRSA held that the implementation of the Final Rule is *not* dependent on any separate implementation of the "must offer" provision via a revision to the Pharmaceutical Pricing Agreement. HRSA further argued that even if the implementation of the Final Rule were dependent on a separate implementation of the "must offer" provision, the Final Rule itself effectively implements that provision, even in the absence of an amendment to the Pharmaceutical Pricing Agreement. Notably, the Final Rule does not contain any "must offer" language.

Additional Implications for Manufacturers of Orphan Designated Drugs

In addition to the concerns raised above regarding operationalizing a price differential based on anticipated use of the product, and about lack of visibility into compliance short of an audit or investigation, manufacturers of orphan drugs should take into consideration three additional risks/concerns.

First, HRSA refused to address manufacturer comments regarding the intersection of this policy choice and the prohibition against off-label promotion. Imagine an orphan product has only one indication for that orphan use. Orphan drug exclusion entities that attempt to purchase the product at the 340B ceiling price are effectively stating that they intend to use the product for a non-indicated use. At what point does the manufacturer's accommodation of that sale become "promotion" that implicates the prohibition against off-label promotion? Does publishing a 340B ceiling price for such a drug amount to improper promotion? Manufacturers should carefully review the way these kinds of sales are made and build in protections against accusations of off label promotion. Highly risk-averse manufacturers may also consider seeking guidance or an Advisory Opinion from HHS OIG for clarity.

Second, orphan drug manufacturers now have an additional incentive to engage with covered entities short of an audit to ensure compliance. Several drug and biologic manufacturers have undertaken covered entity outreach programs in the last several years. These programs are intended to create relationships between the manufacturing and 340B communities, demonstrate to covered entities that manufacturers care about 340B compliance, and provide channels of communication through which noncompliance can be identified and addressed. Manufacturers of orphan drugs should consider informal outreach to the orphan drug exclusion entities in particular to build mutual trust and share compliance best practices.

Third, compliance with the recordkeeping requirements of this rule will be difficult for the orphan drug exclusion covered entities, in that they require specific tracking of each drug dispensed to a patient and for what purpose. If the covered entity cannot adequately track utilization by indication, however, the Final Rule calls for the covered entity to purchase all orphan drugs at non-340B pricing, that is, at WAC or at some non-340B discount. Compliance and tracking by indication will be particularly difficult for covered entities utilizing contract pharmacy arrangements, given that contract pharmacies will not have access to patient records indicating the prescribing physician's intended use. Manufacturers of orphan drugs should pay careful attention to the purchasing and dispensing patterns of orphan drug exclusion covered entities with contract pharmacies where there is greater concern for noncompliance and diversion.

* * * * *

Celebrating more than 125 years of service, King & Spalding is an international law firm that represents a broad array of clients, including half of the Fortune Global 100, with 800 lawyers in 17 offices in the United States, Europe, the Middle East and Asia. The firm has handled matters in over 160 countries on six continents and is consistently recognized for the results it obtains, uncompromising commitment to quality and dedication to understanding the business and culture of its clients. More information is available at www.kslaw.com.

This alert provides a general summary of recent legal developments. It is not intended to be and should not be relied upon as legal advice.

PART 10—340B DRUG PRICING PROGRAM

Subpart A—General Provisions

Subpart B—Eligibility To Purchase 340B Drugs

Subpart C—Drugs Eligible for Purchase under 340B

Authority: Sec. 340B of the Public Health Service Act (42 U.S.C. 256b), as amended; Sec. 215 of the Public Health Service Act (42 U.S.C. 216), as amended; Sec. 526 of the Federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 360bb); Sec. 701(a) of the Federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 371(a)); Sec. 1927 of the Social Security Act, as amended (42 U.S.C. 1396r–8).

Subpart A—General Provisions

§ 10.1 Purpose.

This part implements section 340B of the Public Health Service Act (PHSA) ‘‘Limitation on Prices of Drugs Purchased by Covered Entities.’’

§ 10.2 Summary of 340B Drug Pricing Program.

Section 340B of the PHSA instructs the Secretary of Health and Human Services to enter into agreements with manufacturers of covered drugs under which the amount required to be paid to these manufacturers by certain statutorily-defined entities does not exceed the average manufacturer price for the drug under title XIX of the Social Security Act (SSA) reduced by a rebate percentage which is calculated as indicated in 340B(a)(1) and 340B(a)(2)(A). Manufacturers participating in the 340B Drug Pricing Program (340B Program) are required to provide these discounts on all covered outpatient drugs sold to participating 340B covered entities.

§ 10.3 Definitions.

Ceiling price means the maximum statutory price established under section 340B(a)(1) of the PHSA.

Covered entity means an entity that meets the requirements under section 340B(a)(5) of the PHSA and is listed in section 340B(a)(4) of the PHSA.

Covered outpatient drug has the meaning set forth in section 1927(k) of the SSA.

Group purchasing organization (GPO) is an entity that contracts with purchasers, such as hospitals, nursing homes, and home health agencies, to aggregate purchasing volume and negotiate final prices with manufacturers, distributors, and other vendors.

Manufacturer has the same meaning as set forth in section 1927(k)(5) of the SSA.

Orphan drug means a drug designated by the Secretary under section 526 of the Federal Food, Drug, and Cosmetic Act (FFDCA).

Participating drug manufacturer means a manufacturer that has entered into a Pharmaceutical Pricing Agreement with the Secretary.

Pharmaceutical Pricing Agreement (PPA) means an agreement described in section 340B(a)(1) of the PHSA.

Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom the authority involved has been delegated.

Section 340B means section 340B of the PHSA.

Subpart B—Eligibility To Purchase 340B Drugs

§ 10.10 Entities eligible to participate in the 340B Drug Pricing Program.

Only organizations meeting the definition of a covered entity and listed on the 340B database are eligible to purchase covered outpatient drugs under the 340B Program. A covered entity remains responsible for complying with all other 340B requirements and applicable Federal, state, and local laws.

Subpart C—Drugs Eligible for Purchase Under 340B

§ 10.20 Drugs eligible for purchase under 340B.

The definition of a covered outpatient drug has the meaning given to such term in section 1927(k)(2) of the SSA except as provided in § 10.21 of this part.

§ 10.21 Exclusion of orphan drugs for certain covered entities.

(a) General.

For the covered entities described in paragraph (b) of this section, a covered outpatient drug does not include orphan drugs that 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. A covered outpatient drug includes drugs that are designated under section 526 of the FFDCA when they are transferred, prescribed, sold, or otherwise used for any medically accepted indication other than treating the rare disease or condition for which the drug was designated under section 526 of the FFDCA.

(b) *Covered entities to which the orphan drug exclusion applies.*

(1) The exclusion of orphan drugs when used to treat the rare disease or condition for which the drug was designated under section 526 of the FFDCA from the definition of covered outpatient drugs described in paragraph (a) of this section shall only apply to the following covered entities: free-standing cancer hospitals qualifying under section 340B(a)(4)(M) of the PHSA, critical access hospitals qualifying under section 340B(a)(4)(N) of the PHSA, and rural referral centers and sole community hospitals qualifying under section 340B(a)(4)(O) of the PHSA. The exclusion does not apply to the remaining covered entities that meet the 340B Program eligibility requirements.

(2) When an entity described in this paragraph (b) meets more than one eligibility criterion as a covered entity, the entity shall select its eligibility type and notify the Secretary. These eligible entities are limited to participating in the 340B Program under only one covered entity hospital type and shall abide by all applicable restrictions and requirements for that entity type. A covered entity subject to this provision may only change its participation type to another hospital entity type on a quarterly basis upon express written confirmation from the Secretary.

(c) *Covered entity responsibility to maintain records of compliance.*

(1) A covered entity listed in paragraph (b) of this section is responsible for ensuring that any orphan drugs purchased through the 340B Program are not transferred, prescribed, sold, or otherwise used for the rare condition or disease for which the orphan drugs are designated under section 526 of the FFDCA. A covered entity listed in paragraph (b) of this section that purchases orphan drugs under the 340B Program is required to maintain and provide auditable records on request which document the covered entity's compliance with this requirement available for audit by the Federal Government or, with Federal Government approval, by the manufacturer.

(2) A covered entity may develop an alternative system by which it can prove compliance. Any alternate system must be approved by the Secretary prior to implementation. Each alternate system of compliance will be reviewed on a case-by-case basis.

(3) A covered entity listed in paragraph (b) of this section that cannot or does not wish to maintain auditable records sufficient to demonstrate compliance with this rule, must notify HRSA and purchase all orphan drugs outside of the 340B Program regardless of the indication for which the drug is used. Once a hospital is enrolled in 340B, it may change its decision to purchase all orphan drugs outside of the 340B Program on a quarterly basis by notifying HRSA. This documentation will be made public. This information will also be verified during the annual recertification process.

(d) *Use of group purchasing organizations by a free-standing cancer hospital.*

(1) A free-standing cancer hospital enrolled under section 340B(a)(4)(M) must also comply with the prohibition against using a GPO under section 340B(a)(4)(L)(iii) of the PHSA for the purchase of any covered outpatient drug.

(2) A covered entity that is a freestanding cancer hospital cannot use a GPO to purchase orphan drugs when they are transferred, prescribed, sold, or otherwise used for an indication other than the rare condition or disease for which that orphan drug was designated under section 526 of the FFDCA.

(3) A covered entity that is a freestanding cancer hospital may use a GPO for purchasing orphan drugs when orphan drugs are transferred, prescribed, sold, or otherwise used for the rare disease or condition for which it was designated under section 526 of the FFDCA.

(4) If a covered entity that is a freestanding cancer hospital chooses to use a GPO for purchasing an orphan drug used for a rare disease or condition for which it is designated, it is required to maintain auditable records that demonstrate full compliance with the orphan drug purchasing requirements and limitations. A free-standing cancer hospital covered entity that cannot or does not wish to maintain auditable records sufficient to demonstrate compliance, must notify HRSA and purchase all orphan drugs outside of the 340B Program, regardless of indication for which the drug is used, and is not permitted to use a GPO to purchase those drugs. Once a free-standing cancer hospital is enrolled in 340B, it may change its decision to purchase all orphan drugs outside of the 340B Program on a quarterly basis by notifying HRSA. This documentation will be made public. This information will also be verified during the annual recertification process.

(e) *Identification of orphan drugs.*

Designations under section 526 of the FFDCA are the responsibility of and administered by the FDA. Only covered outpatient drugs that match the listing and sponsor of the orphan designation are considered orphan drugs for purposes of this section. HRSA will publish on its public Web site FDA's section 526 list of drugs that will govern the next quarter's purchases.

(f) *Failure to comply.*

Failure to comply with this section shall be considered a violation of sections 340B(a)(5) and 340B(e) of the PHSA, as applicable.