DEPARTMENT OF HEALTH AND HUMAN SERVICES

OFFICE OF INSPECTOR GENERAL

WASHINGTON, DC 20201

[*We redact certain identifying information and certain potentially privileged, confidential, or proprietary information, unless otherwise approved by the requestor(s).*]

Issued: December 22, 2022

Posted: December 28, 2022

[Address block redacted]

Re: OIG Advisory Opinion No. 22-22

Dear [redacted]:

The Office of Inspector General ("OIG") is writing in response to your request for an advisory opinion on behalf of [redacted] ("Requestor") regarding Requestor's proposal to provide up to a specified number of trial units of a long-acting antipsychotic drug to certain hospitals for inpatient use (the "Proposed Arrangement"). Specifically, you have inquired whether the Proposed Arrangement, if undertaken, would constitute grounds for the imposition of sanctions under the exclusion authority at section 1128(b)(7) of the Social Security Act (the "Act") or the civil monetary penalty provision at section 1128A(a)(7) of the Act, as those sections relate to the commission of acts described in section 1128B(b) of the Act (the "Federal anti-kickback statute").

Requestor has certified that all of the information provided in the request, including all supplemental submissions, is true and correct and constitutes a complete description of the relevant facts and agreements among the parties in connection with the Proposed Arrangement, and we have relied solely on the facts and information you provided. We have not undertaken an independent investigation of the certified facts and information presented to us by Requestor. This opinion is limited to the relevant facts presented to us by Requestor in connection with the Proposed Arrangement. If material facts have not been disclosed or have been misrepresented, this opinion is without force and effect.

Based on the relevant facts certified in your request for an advisory opinion and supplemental submissions, we conclude that, although the Proposed Arrangement, if undertaken, would generate prohibited remuneration under the Federal anti-kickback statute if the requisite intent were present, the OIG would not impose administrative sanctions on Requestor under sections 1128A(a)(7) or 1128(b)(7) of the Act, as those sections relate to the commission of acts described in the Federal anti-kickback statute.

This opinion may not be relied on by any person[1] other than Requestor and is further qualified as set out in Part IV below and in 42 C.F.R. Part 1008.

I. FACTUAL BACKGROUND

A. The Drug

Requestor manufactures [redacted] (the "Drug"), which is a long-acting injectable ("LAI") atypical antipsychotic drug approved by the U.S. Food & Drug Administration ("FDA") for the treatment of adults with [redacted] (the "Disorder"). Requestor cited to various peer-reviewed articles that indicate that medication nonadherence is common for patients with the Disorder. Requestor explained that nonadherence leads to negative outcomes among patients with the Disorder, such as an exacerbation of symptoms, increased rates of hospitalization, and longer lengths of hospital stays, all of which could increase costs to the health care system. LAI formulations, such as the Drug, can provide uninterrupted medication coverage for an extended period of time, which, according to Requestor, reduces the incidence of nonadherence and thus reduces the risk of these outcomes. The Drug is dosed on a once-monthly basis. Requestor cited studies that found that, after being discharged from an inpatient stay, patients treated with LAI antipsychotics had significantly lower readmission rates than patients treated with daily oral antipsychotics. Other studies cited by Requestor found that patients taking LAI antipsychotics were more likely to be adherent than those taking an oral counterpart and that LAI antipsychotics can prevent any abrupt loss of efficacy that may occur in the event of a missed dose of a daily oral antipsychotic.

A health care professional administers the Drug by subcutaneous injection in either an inpatient or outpatient setting. When administered in an inpatient setting, it generally is not separately reimbursable by a Federal health care program, and Requestor is not aware of a Federal health care program that imposes a separate cost-sharing obligation specific to the Drug; for example, under Medicare Part A, the Drug treatment is included within the overall payment for the applicable Medicare Severity Diagnosis-Related Group for the patient's stay.[2] When administered to Medicare patients in the outpatient setting, the Drug is covered by either Medicare Part B or Part D, depending on the setting in which the Drug is dispensed. In either circumstance, Medicare patients treated with the Drug are subject to any applicable cost-sharing obligations.

Requestor certified that there are more than seven competing LAI atypical antipsychotics that rely on various active ingredients. There also are multiple generic oral antipsychotics using the

---

[1] We use "person" herein to include persons, as referenced in the Federal anti-kickback statute, as well as individuals and entities, as referenced in the exclusion authority at section 1128(b)(7) of the Act.

[2] Generally, Federal health care programs reimburse for inpatient services on a prospective basis, but Requestor noted that some state Medicaid programs may pay on a per diem or a cost basis, and some facility types (e.g., critical access hospitals) are paid for inpatient services based on a percentage of reasonable costs.

same active ingredient as the Drug. According to Requestor, as of August 2022, the list prices for typical doses of the LAI atypical antipsychotics currently on the market generally range from about $850 to $3,100 for one month of treatment. As of August 2022, median list prices for typical doses of generic formulations of oral antipsychotics using the same active ingredient as the Drug generally range from about $0.32 to $0.75 per day (or approximately $9.60 to $22.50 per month).

The Drug's label instructs prescribers first to establish tolerability to the Drug's active ingredient via an oral formulation of that same active ingredient for patients who have never taken the active ingredient.[3] After establishing tolerability, a patient who receives an injection of the first dose of the Drug would not require any supplemental oral medication for the Drug to be effective. Requestor also certified that, although the Drug does not require an initial "loading dose" of oral antipsychotics (i.e., a dose of oral antipsychotics taken for a number of days after an initial LAI injection), many individuals admitted to hospitals for emergency psychiatric episodes receive oral antipsychotic treatment during the acute phase of their stay, which typically lasts up to 3 days, and only later are evaluated for LAI antipsychotics. Inpatient stays with a principal diagnosis of the Disorder had, as of 2016 data, an average length of stay of 10.5 days.[4]

B. The Proposed Arrangement

Under the Proposed Arrangement, Requestor would permit hospitals that do not accept and dispense samples that comply with the Prescription Drug Marketing Act of 1987 ("PDMA")[5] in their facilities[6] to request up to a maximum number of 20 units per month, limited to 2 free units of the Drug (each of which provides medication coverage for 1 month) per eligible inpatient, per calendar year. The ordering system would prevent a pharmacist from placing an order that would result in the delivery of units beyond the hospital's limit.

To receive free trial units of the Drug, a hospital would be required to register and enroll in the Proposed Arrangement (a "Participating Hospital") through an online portal, and continued participation would require annual renewal. Upon enrollment in the program, the program administrator would initially ship to the Participating Hospital up to five free trial doses of the

---

[3] According to Requestor, a typical trial to establish tolerability involves two doses of an oral antipsychotic, administered 24 hours apart.

[4] Pamela L. Owens et al., Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project, Statistical Brief #249: Inpatient Stays Involving Mental and Substance Use Disorders, 2016 11 (Mar. 2019), https://www.hcup-us.ahrq.gov/reports/statbriefs/sb249-Mental-Substance-Use-Disorder-Hospital-Stays-2016.pdf.

[5] See 21 U.S.C. § 353.

[6] Requestor certified that hospitals have various reasons for permitting programs like the Proposed Arrangement while refusing to permit PDMA sample programs. For example, PDMA-compliant samples may be given by a sales representative to a physician, which could violate the protocols of some hospitals because those samples would bypass the hospital pharmacies.

Drug based on the request of the Participating Hospital's pharmacist. After trial units are administered to eligible inpatients, the pharmacist would be able to order units of the Drug to replace those administered, such that, at any given time, a Participating Hospital would have no more than a maximum of five units in inventory as part of the Proposed Arrangement. Replacement trial units of the Drug would be ordered through the secure online portal, subject to the certification requirements described below.

Requestor would make hospitals aware of the Proposed Arrangement via: (i) field-based sales representatives; (ii) Requestor-approved communications sent directly to hospitals; or (iii) prescriber-accessible websites. The Proposed Arrangement would not be advertised in magazines, journals, digital ads, or other mass consumption forums. Requestor certified that the Proposed Arrangement would not give prescribers any financial incentive to prescribe the Drug to inpatients as opposed to a competing LAI or a daily oral alternative.

As part of the enrollment and renewal process, and on each acknowledgment form that Participating Hospitals must complete upon receipt of each free trial unit shipment of the Drug, each Participating Hospital would be required to certify that it will comply with certain terms and conditions, which include the following:

- Participating Hospital employees understand the FDA-approved indications for the Drug;
- Participating Hospitals may only administer the Drug to inpatients for use consistent with the Drug's label;
- Participating Hospitals will require that prescribers act in accordance with professional standards, including making decisions to prescribe the Drug in the best interest of the patient;
- the Drug may be administered to a patient only if the prescriber has independently determined that the Drug is clinically appropriate for that patient and that immediate onsite treatment with the Drug increases the long-term likelihood of a positive treatment outcome;
- there is no obligation on the part of a Participating Hospital or prescriber to continue using, prescribing, or recommending the Drug, or any other drug, as a condition of receiving a trial unit;
- neither the Participating Hospital nor the administering practitioner bills any patient, insurer, or other third party for the free Drug or for any administration services in connection with the free Drug, and the free units may not be sold, resold, traded, or distributed for sale;
- the Participating Hospital does not accept PDMA-compliant samples, and the Participating Hospital will notify Requestor if that position changes;
- the Participating Hospital and its pharmacy must have the ability to track utilization of the free trial units of the Drug received under the Proposed Arrangement by each patient and establish adequate controls to ensure that such units are appropriately segregated and tracked; and

- the Participating Hospital will conduct certain monitoring to detect irregularities, such as failure to comply with the terms and conditions of participation or to submit forms acknowledging receipt of the free Drug.

Participating Hospitals would complete and submit a request for trial units through a secure online portal. To place an order for additional free trial units, the Participating Hospital's pharmacist would be required to certify that each of the free trial units the Participating Hospital wishes to replace was administered to an eligible inpatient consistent with the Drug's labeled indication. Specifically, for each administered trial unit, the pharmacist would be required to provide the date of administration of each trial unit and confirm that the patient was 18 years of age or older and had a diagnosis of the Disorder. The program administrator would validate each product order to confirm eligibility of the Participating Hospital and ensure that the required certifications were submitted and then would ship the requested free trial units directly to the pharmacy that dispenses products for a Participating Hospital's inpatient use.

Upon receiving free trial units, the Participating Hospital would be required to sign and return a shipment receipt and acknowledgment form to the program administrator.[7] When free trial units are sent to a Participating Hospital's designated pharmacy, the packaging would include a notification that reiterates that no free units of the Drug may be sold, resold, traded, distributed for sale, or billed to any insurer or Federal health care program.

For a patient to be eligible to receive the free Drug: (i) the patient must have been diagnosed with the Disorder; (ii) the administration of the Drug to the patient must be consistent with the Drug's label; and (iii) the patient must be a current inpatient at a Participating Hospital.

If a Medicare beneficiary who received a free trial unit as an inpatient continued to be prescribed the Drug after discharge, as noted above, the Drug generally would be covered by Medicare Part B or D, as appropriate, and subject to any applicable cost-sharing amounts. However, Requestor certified that patients would not be obligated to continue using the Drug after discharge or upon conclusion of their eligibility to receive the free Drug. In addition, Requestor certified that there are no known clinical barriers to transitioning from the Drug to another LAI or oral antipsychotic medication.

II. LEGAL ANALYSIS

A. Law

The Federal anti-kickback statute makes it a criminal offense to knowingly and willfully offer, pay, solicit, or receive any remuneration to induce, or in return for, the referral of an individual to a person for the furnishing of, or arranging for the furnishing of, any item or service reimbursable under a Federal health care program.[8] The statute's prohibition also extends to

[7] Requestor certified that an experienced third-party vendor would administer the Proposed Arrangement.

[8] Section 1128B(b) of the Act.

remuneration to induce, or in return for, the purchasing, leasing, or ordering of, or arranging for or recommending the purchasing, leasing, or ordering of, any good, facility, service, or item reimbursable by a Federal health care program.[9] For purposes of the Federal anti-kickback statute, "remuneration" includes the transfer of anything of value, directly or indirectly, overtly or covertly, in cash or in kind.

The statute has been interpreted to cover any arrangement where one purpose of the remuneration is to induce referrals for items or services reimbursable by a Federal health care program.[10] Violation of the statute constitutes a felony punishable by a maximum fine of $100,000, imprisonment up to 10 years, or both. Conviction also will lead to exclusion from Federal health care programs, including Medicare and Medicaid. When a person commits an act described in section 1128B(b) of the Act, the OIG may initiate administrative proceedings to impose civil monetary penalties on such person under section 1128A(a)(7) of the Act. The OIG also may initiate administrative proceedings to exclude such person from Federal health care programs under section 1128(b)(7) of the Act.

B. Analysis

At the outset, we note that providing drug samples is a widespread industry practice, and the PDMA governs their distribution. As we explained in the OIG Compliance Program Guidance for Pharmaceutical Manufacturers:

> [F]ailure to comply with the requirements of PDMA can result in sanctions. In some circumstances, if the samples have monetary value to the recipient (e.g., a physician) and are used to treat [F]ederal health care program beneficiaries, the improper use of samples may also trigger liability under other statutes, including the False Claims Act and the anti-kickback statute.[11]

Requestor certified that the Proposed Arrangement would be limited to hospitals that do not accept PDMA-compliant samples. We express no opinion regarding Requestor's potential liability under the PDMA or the False Claims Act; this opinion is limited to the OIG's administrative authorities relating to the Federal anti-kickback statute.

The Proposed Arrangement would implicate the Federal anti-kickback statute because the free trial units would constitute remuneration that Requestor offers and provides to hospitals, and hospitals may be referral sources for the Drug. For example, hospitals often establish formularies that limit or influence the drugs that prescribers may administer or dispense to inpatients and thus are in a position to arrange for or recommend purchases of the Drug.

---

[9] Id.

[10] E.g., United States v. Nagelvoort, 856 F.3d 1117 (7th Cir. 2017); United States v. McClatchey, 217 F.3d 823 (10th Cir. 2000); United States v. Davis, 132 F.3d 1092 (5th Cir. 1998); United States v. Kats, 871 F.2d 105 (9th Cir. 1989); United States v. Greber, 760 F.2d 68 (3d Cir. 1985).

[11] OIG Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23,731, 23,739 (May 5, 2003).

Because no safe harbor is available to protect the Proposed Arrangement, we evaluate the facts and circumstances of the Proposed Arrangement and assess risks such as overutilization, increased costs to Federal health care programs, corruption of medical decision-making, patient steering, and unfair competition. For the combination of the following reasons, we believe that the risk under the Federal anti-kickback statute would be sufficiently low.

First, the risk of a Participating Hospital steering inpatients to the Drug based on receipt of the Drug for free under the Proposed Arrangement is low. Participating Hospitals would be required to permit clinicians to make independent decisions about whether the Drug is clinically appropriate for a particular patient, and the Proposed Arrangement would not give prescribers any financial incentive to prescribe the Drug to inpatients as opposed to a competing LAI antipsychotic or a daily oral alternative. While a prescriber would be able to benefit financially from prescribing the Drug on an outpatient basis where the Drug is a billable, physician-administered drug, that benefit would occur even absent the Proposed Arrangement, and prescribers could receive a comparable benefit if prescribing a different LAI antipsychotic.[12] According to Requestor, there are more than seven competing LAI atypical antipsychotics currently available on the market. In addition, Requestor certified that there is no known clinical barrier to a patient switching to another LAI or oral antipsychotic medication after receiving the Drug. While we recognize that a Participating Hospital may avoid some costs of administering a daily oral antipsychotic for the duration of the patient's stay, the Participating Hospital would still need to administer oral antipsychotic drugs for many patients before administering the Drug, either during the acute phase of an inpatient stay or to establish tolerability to the active ingredient.

Second, the Proposed Arrangement would be unlikely to increase costs to Federal health care programs inappropriately and could reduce program costs over time if the Drug successfully achieves the outcomes cited by Requestor. Requestor certified that, under the Proposed Arrangement, Participating Hospitals agree to give the free trial units of the Drug only to patients diagnosed with the Disorder and for whom a prescriber independently determined that: (i) the Drug is clinically appropriate; and (ii) immediate onsite treatment with the Drug increases the long-term likelihood of a positive treatment outcome. Requestor also provided information about peer-reviewed studies showing that LAI antipsychotics, like the Drug, reduce the risk of negative outcomes, such as hospitalizations. We recognize that the Drug could be billed to Federal health care programs if a beneficiary continues to receive it after discharge. However, to the extent that treatment using LAI antipsychotics, such as the Drug, could reduce incidences of nonadherence and the risk of negative outcomes (e.g., hospitalizations), aggregate costs to Federal health care programs and beneficiaries could decrease over time.

Third, the Proposed Arrangement would include a number of safeguards to minimize the risk that the free trial units would be misused. For example, the Participating Hospital would be required to agree that the trial units cannot be sold, resold, traded, distributed for sale, or billed to

[12] The Proposed Arrangement would include only free trial units to the Participating Hospital for treatment of eligible inpatients, not any units of the Drug administered in an outpatient setting. In the outpatient setting where the Drug and its administration can be billed, the usual cost-control features, including any beneficiary cost-sharing obligations, would apply.

any patient or payor. Participating Hospitals could receive only a limited number of trial units per year and per patient. By participating in the Proposed Arrangement, Participating Hospitals would agree that they: (i) will require that prescribers act in accordance with professional standards, including making prescribing decisions in the best interest of the patient; and (ii) understand that neither the prescriber nor the Participating Hospital are under any obligation to continue using, prescribing, or recommending the Drug, or any other drug, as a condition of receiving a trial unit.

III. CONCLUSION

Based on the relevant facts certified in your request for an advisory opinion and supplemental submissions, we conclude that, although the Proposed Arrangement, if undertaken, would generate prohibited remuneration under the Federal anti-kickback statute if the requisite intent were present, the OIG would not impose administrative sanctions on Requestor under sections 1128A(a)(7) or 1128(b)(7) of the Act, as those sections relate to the commission of acts described in the Federal anti-kickback statute.

IV. LIMITATIONS

The limitations applicable to this opinion include the following:

- This advisory opinion is limited in scope to the Proposed Arrangement and has no applicability to any other arrangements that may have been disclosed or referenced in your request for an advisory opinion or supplemental submissions.

- This advisory opinion is issued only to Requestor. This advisory opinion has no application to, and cannot be relied upon by, any other person.

- This advisory opinion may not be introduced into evidence by a person other than Requestor to prove that the person did not violate the provisions of sections 1128, 1128A, or 1128B of the Act or any other law.

- This advisory opinion applies only to the statutory provisions specifically addressed in the analysis above. We express no opinion herein with respect to the application of any other Federal, state, or local statute, rule, regulation, ordinance, or other law that may be applicable to the Proposed Arrangement, including, without limitation, the physician self-referral law, section 1877 of the Act (or that provision's application to the Medicaid program at section 1903(s) of the Act).

- This advisory opinion will not bind or obligate any agency other than the U.S. Department of Health and Human Services.

- We express no opinion herein regarding the liability of any person under the False Claims Act or other legal authorities for any improper billing, claims submission, cost reporting, or related conduct.

This opinion is also subject to any additional limitations set forth at 42 C.F.R. Part 1008.

The OIG will not proceed against Requestor with respect to any action that is part of the Proposed Arrangement taken in good faith reliance upon this advisory opinion, as long as all of the material facts have been fully, completely, and accurately presented, and the Proposed Arrangement in practice comports with the information provided. The OIG reserves the right to reconsider the questions and issues raised in this advisory opinion and, where the public interest requires, to rescind, modify, or terminate this opinion. In the event that this advisory opinion is modified or terminated, the OIG will not proceed against Requestor with respect to any action that is part of the Proposed Arrangement taken in good faith reliance upon this advisory opinion, where all of the relevant facts were fully, completely, and accurately presented and where such action was promptly discontinued upon notification of the modification or termination of this advisory opinion. An advisory opinion may be rescinded only if the relevant and material facts have not been fully, completely, and accurately disclosed to the OIG.

Sincerely,

/Robert K. DeConti/

Robert K. DeConti
Assistant Inspector General for Legal Affairs