No. 15-3805

IN THE UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

GERASIMOS PETRATOS, et al.,

Plaintiffs-Appellants,

v.

GENENTECH INC., et al.,

Defendants-Appellees.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

BRIEF FOR THE UNITED STATES OF AMERICA AS AMICUS CURIAE IN SUPPORT OF NEITHER PARTY

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INTEREST OF THE UNITED STATES

The False Claims Act (FCA), 31 U.S.C. § 3729 *et seq.*, is the federal government's primary tool to combat fraud and recover losses due to fraud in federal programs. Accordingly, the United States has a substantial interest in the proper interpretation of the FCA. The United States also administers the Medicare and Medicaid programs, and therefore has a substantial interest in the proper interpretation of the statutes, regulations, and guidance that govern those programs.

The United States submits this amicus brief to address three holdings of the district court that involve the application of the FCA to Medicare, Medicaid, and other government programs. The district court correctly recognized that violations of FDA adverse-event-reporting regulations can, in rare instances, create FCA liability. The court erred, however, by holding that drugs prescribed for FDA-approved and other "medically accepted" indications are per se "reasonable and necessary" for purposes of Medicare and Medicaid reimbursement. The court also erred by precluding the possibility of FCA liability for fraud that induces physicians

to prescribe drugs paid for by the United States. The government takes no position on whether the allegations in the relator's complaint are sufficient to survive dismissal.

STATEMENT OF THE CASE

A. The False Claims Act

The False Claims Act is "the Government's primary litigative tool" for combatting fraud, and was intended "to reach all fraudulent attempts to cause the Government to pay out sums of money." S. Rep. No. 99-345, at 2, 9 (1986). Congress therefore drafted the statute "expansively . . . 'to reach all types of fraud, without qualification, that might result in financial loss to the Government.'" *Cook Cty. v. United States ex rel. Chandler*, 538 U.S. 119, 129 (2003).

An FCA violation occurs when a person "knowingly presents, or causes to be presented, a false or fraudulent claim for payment or approval." 31 U.S.C. § 3729(a)(1)(A). A violation also occurs when a person "knowingly makes, uses, or causes to be made or used, a false

record or statement material to a false or fraudulent claim." *Id.* § 3729(a)(1)(B).[1]

The FCA authorizes suits to collect statutory damages and penalties either by the Attorney General or by a private person (known as a *qui tam* relator) in the name of the United States. 31 U.S.C. § 3730(a), (b)(1); *see also Vermont Agency of Nat. Res. v. United States ex rel. Stevens*, 529 U.S. 765, 769-78 (2000). If a relator files a *qui tam* action, the government may intervene and take over the case. 31 U.S.C. § 3730(b)(2). If the government declines to intervene, the relator conducts the litigation. *Id.* § 3730(c)(3). Monetary

[1] The current version of these provisions took effect on May 20, 2009, after passage of the Fraud Enforcement and Recovery Act of 2009, Pub. L. No. 111-21, § 4, 123 Stat. 1617, 1621-25. The prior version had some differences in wording. *See* 31 U.S.C. § 3729(a)(1) (2006) (creating liability for any person who "knowingly presents, or causes to be presented" to a federal employee or official "a false or fraudulent claim for payment or approval"); *id.* § 3729(a)(2) (creating liability for any person who "knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the Government"). The principal allegations in the complaint post-date the 2009 amendments, *see, e.g.*, A269-70 (Am. Compl. ¶ 6), A304-41 (Am. Compl. ¶¶ 128-244), and the parties do not appear to dispute that the amended version of the statute applies.

proceeds from a *qui tam* suit are divided between the government and the relator. *Id.* § 3730(d).

B. Adverse Event Reporting to FDA

Under the Federal Food, Drug, and Cosmetic Act, the Food and Drug Administration (FDA) must approve a drug before a manufacturer can market the drug in the United States. FDA will approve a new drug application only after determining, among other things, that the new drug is safe and effective for its intended use. *See generally* 21 U.S.C. § 355.

Even after approval, FDA retains responsibility to revoke that approval under certain circumstances. For example, FDA must revoke approval when data shows "that [the] drug is unsafe for use" or when new information demonstrates there is no longer sufficient evidence to establish the drug's safety or efficacy. 21 U.S.C. § 355(e). To enable FDA to make these and other determinations, pharmaceutical companies with approved drug applications are required to submit reports of adverse events associated with those drugs to FDA. *See* 21 C.F.R. §§ 314.80, 314.98(a); *see also* 21 U.S.C. § 355(k)(1)-(3) (authorizing regulations governing the

collection and reporting of data); 21 U.S.C. § 331(e). Serious and unexpected adverse events must be reported to FDA within fifteen calendar days from initial receipt of the information. *See* 21 C.F.R. § 314.80(c)(1)(i). Other adverse events, including serious events already accounted for in a drug's labeling, must be reported to FDA via periodic reports. *See id.* § 314.80(c)(2). If a pharmaceutical company fails to comply with the adverse-event-reporting requirements, FDA may initiate proceedings to withdraw approval of the drug, seek an injunction, or pursue criminal prosecution. *See* 21 U.S.C. §§ 332, 333(a), 355(e).

C. Requirements for Reimbursement Under Medicare Parts A and B

Medicare Parts A and B, which are administered by the Centers for Medicare and Medicaid Services (CMS) within the Department of Health and Human Services (HHS), operate principally by reimbursing health care providers for the cost of medical care provided to program beneficiaries.

Among other requirements, the Medicare statute expressly prohibits reimbursement for items and services that "are not reasonable and

necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." 42 U.S.C. § 1395y(a)(1)(A).

Physicians and other qualified medical providers provide the first line of defense in enforcing the "reasonable and necessary" requirement. Medicare regulations explain that "[t]he physician has a major role in determining utilization of health services furnished by providers. The physician decides upon admissions, orders tests, drugs, and treatments, and determines the length of stay." 42 C.F.R. § 424.10(a). In many contexts, Medicare also requires physicians to make specific certifications. For Medicare Parts A and B, it is "a condition for Medicare payment that a physician certify the necessity of the services and, in some instances, recertify the continued need for those services." *Id.*; *see also* 42 U.S.C. § 1395f(a)(2)-(3) (Part A); 42 U.S.C. § 1395n(a)(2) (Part B). *But see, e.g.*, 42 U.S.C. § 1395n(a)(2)(B) (exceptions to certification requirement); 42 C.F.R. § 424.24(a) (same).

For example, to obtain reimbursement for physician-administered drugs under Medicare Part B, a physician must prescribe the treatment,

have it administered under his or her supervision, and then submit a reimbursement request to Medicare. On the reimbursement form, the physician must expressly certify that the treatment was "medically necessary and personally furnished by me or . . . my employee under my direct supervision." CMS Form 1500, https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/Downloads/CMS1500.pdf.[2]

CMS has the ultimate authority to determine whether a treatment is "reasonable and necessary" for purposes of reimbursement under Medicare Parts A and B. CMS or its contractors can make such a determination by several means.[3] First, CMS can make a "national coverage determination," which determines "whether or not a particular item or service is covered nationally." 42 U.S.C. § 1395y(l)(6)(A). Second, the administrative contractors responsible for reviewing Medicare claims

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[2] This certification is not required if the drug is furnished by a hospital "incident to physicians' services furnished to outpatients." 42 C.F.R. § 424.24(a)(1).

[3] Due primarily to the volume of claims, Medicare claims processing is largely an automated process. Only a small subset of claims receives individual review, which is typically triggered by a systems edit or prepayment review.

can make "local coverage determination[s]," which determine whether a treatment is covered for claims within that contractor's responsibility. *Id.* §§ 1395y(l)(6)(B), 1395ff(f)(2)(B). Third, contractors can make determinations on a claim-by-claim basis. *Id.* § 1395ff(a)(1)(A). Each type of determination is subject to multiple levels of review. *See id.* § 1395ff(a)(3), (b)-(d), (f), (i).

One key consideration in the "reasonable and necessary" determination under Medicare Parts A and B is whether the drug has been approved by FDA. CMS guidance for Medicare Parts A and B explains that, with some exceptions, a drug must have final marketing approval from FDA to be considered "reasonable and necessary." *See* Medicare Benefit Policy Manual, CMS Pub. 100-2, ch. 1, § 30 (Part A), https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals-Ioms-Items/Cms012673.html (A118-19); *id.* § 30.2; *id.* ch. 15, §§ 50.4, 50.4.5 (Part B). CMS will not reimburse for a drug if FDA determines that a drug is "less than effective" for all labeled indications. *Id.*

ch. 15, §§ 50, 50.4.6 (Part B); *see id.* ch. 1, § 30 (applying Part B guidance to Part A).

In many instances, a drug must also be used for a "medically accepted" indication—one that is approved by FDA or supported by certain third-party compendia or other authorities. *See* 42 U.S.C. § 1395x(t)(2) (discussing drugs used in an anticancer chemotherapeutic regimen); 42 C.F.R. § 414.930 (relevant compendia for drugs used in an anticancer chemotherapeutic regimen); Medicare Benefit Policy Manual ch. 15, §§ 50.4.2, 50.4.5 (discussing drugs used for unapproved indications).

FDA approval is only one of the criteria relevant to whether use of a drug is "reasonable and necessary," however. The treatment must also be "reasonable and necessary *for [the] individual patient*," a determination made "with reference to accepted standards of medical practice and the medical circumstances of the individual case." *See* Medicare Benefit Policy Manual, ch. 15, § 50.4.3 (emphasis added). The treatment must also satisfy other criteria, including that "the route of administration is medically reasonable and necessary." *Id.* ch. 15, § 50.2 (Part B). CMS may therefore

find that a drug is not "reasonable and necessary" even when used for an FDA-approved indication. *See id.* ch. 15, § 50.4.3 (offering examples).[4]

D. The Present Litigation

1. The relator in this *qui tam* action is Gerasmos Petratos, a former head of healthcare data analytics for Genentech. A275 (Am. Compl. ¶ 24).[5]

[4] Unlike Medicare Parts A and B, Medicare Part D plans are designed and administered in the first instance by third-party plan sponsors that contract with CMS, and Medicaid plans are administered by the states. Different plans may therefore have different requirements for reimbursement. The statutes, regulations, and guidance that govern these plans incorporate some requirements similar to those discussed above for Parts A and B. A doctor's prescription is generally required for drug coverage under Medicare Part D or Medicaid. 42 U.S.C. §§ 1395w-102(e)(1)(A), 1396r-8(k)(2)(A), (k)(4); 42 C.F.R. § 423.104(h). FDA approval is a further precondition for coverage and payment, with certain narrow exceptions. *See* 42 U.S.C. § 1396r-8(k)(2)(A) (defining "covered outpatient drug" for Medicaid purposes); *id.* § 1395w-102(e)(1) (relying in part on Medicaid definition for Medicare Part D). As with Parts A and B, Part D and Medicaid plans may deny coverage on necessity grounds even if a drug is prescribed for an FDA-approved indication. *See* 42 U.S.C. § 1395w-102(e)(3)(A) (stating that Part D plan "may" exclude from coverage items that would not be "reasonable and necessary" under the Parts A and B definition); 42 C.F.R. § 440.230 (stating that Medicaid plans "may" limit service based on "medical necessity"); *see also* 42 U.S.C. § 1396r-8(d)(4)(C); 42 C.F.R. § 456.705.

Genentech owns Avastin, a widely-prescribed drug approved by FDA for the treatment of several types of cancer. A293-97 (Am. Compl. ¶¶ 89-101).

Petratos's amended complaint alleges that Genentech suppressed information about Avastin's side effects after it was approved by FDA. A300-04 (Am. Compl. ¶¶ 115-127). The complaint alleges that Genentech did so in part by basing its FDA-mandated adverse-event-reporting on third-party patient databases that lacked the data necessary for proper analysis of Avastin's side effects. A304-19 (Am. Compl. ¶¶ 128-166). Although other databases had more complete information and would have allowed such analysis, Genentech allegedly declined to use them because of the "business risk" of uncovering negative information about Avastin. *Id.*

Petratos also alleges that Genentech stopped him from conducting analyses using these other databases that would have demonstrated that proteinuria—a buildup of protein in the kidneys—was more common than

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[5] The complaint also names as defendants three companies related to the Roche Group, which now owns Genentech. A278 (Am. Compl. ¶ 39-40). For simplicity, this brief refers only to Genentech.

previously reported. A297 (Am. Compl. ¶ 103), A314-19 (Am. Compl. ¶¶ 154-166). Genentech also allegedly misrepresented to a "key opinion leader" that Genentech lacked sufficient data to answer inquiries about proteinuria, when in fact it did possess such data, A321-23 (Am. Compl. ¶¶ 175-181), and it declined to conduct a study of that data that would have demonstrated whether proteinuria was dependent on the dose of Avastin given, A323 (Am. Compl. ¶¶ 179-180).

Petratos further alleges that Genentech delayed reporting deaths and other adverse events from post-approval clinical trials until the trials were over and that it failed to adequately investigate adverse events. A319-21 (Am. Compl. ¶¶ 167-174), A326 (Am. Compl. ¶ 188).

Finally, Petratos alleges that Genentech submitted reports in connection with FDA proceedings to withdraw Avastin's approval for metastatic breast cancer that misrepresented or omitted information about the incidence, dose-dependence, and reversibility of proteinuria. A333-37 (Am. Compl. ¶¶ 213-229). Those proceedings ended with the withdrawal of Avastin's indication for metastatic breast cancer. A337 (Am. Compl.

¶ 229). Petratos alleges that Genentech also submitted reports to European regulators that omitted relevant data and safety assessments and misrepresented the risk of side effects. A329-32 (Am. Compl. ¶¶ 200-212). And in response to a CMS request for data for use in setting reimbursement rates, Genentech allegedly relied on data sources that underreported the incidence of side effects and therefore the costs of using Avastin. A337-40 (Am. Compl. ¶¶ 230-237).

Petratos alleges that, absent Genentech's misconduct, the government would have reimbursed for Avastin at lower rates, for lower dosages, or not at all. A274 (Am. Compl. ¶ 19), A341-42 (Am. Compl. ¶¶ 243, 246). He also alleges that the warnings on Avastin's FDA-approved label would have changed. A274 (Am. Compl. ¶ 19), A323 (Am. Compl. ¶ 180). Finally, Petratos alleges that, had Genentech disclosed accurate information about Avastin to the medical community, doctors would have determined that Avastin was not medically necessary, or not medically necessary at the recommended dosage, for some of their patients, particularly those at high risk for side effects. A272-74 (Am. Compl. ¶¶ 16, 19), A340-42 (Am. Compl.

¶¶ 239-242, 246). Physicians would therefore have prescribed lower doses of Avastin or not prescribed Avastin at all, resulting in fewer or smaller claims for government reimbursement. A270 (Am. Compl. ¶ 8), A272-74 (Am. Compl. ¶¶ 16, 19), A340-43 (Am. Compl. ¶¶ 238-242, 246, 250).

2. The district court dismissed the relator's amended complaint. A21 (Op.).[6] The court held that Petratos's allegations did not establish that any claims for Medicare or Medicaid reimbursement were "false" within the meaning of the False Claims Act. A5, A17-21 (Op.).

The court rejected the relator's argument that reimbursement claims for Avastin were false because their submission constituted an "implied certification" that Genentech was in compliance with FDA adverse-event-reporting requirements. A17 (Op.). The court explained that, to demonstrate falsity based on regulatory violations, "a plaintiff must show that if the Government had been aware of the" relevant violations, "it would not have paid the defendant's claims." A11 (Op.) (quoting *United*

[6] The court granted Petratos leave to file an amended complaint after dismissing two counts of his original complaint. *See* A41 (1/30/14 Opinion); A58 (12/18/14 Order).

States ex rel. Wilkins v. United Health Grp., Inc., 659 F.3d 295, 307 (3d Cir. 2011)). In this case, the court held, the relator's allegations did not show that Genentech "violated any regulation at all." A18 (Op.). Moreover, the court continued, "[t]here are no factual allegations showing that CMS would not have reimbursed these claims had these deficiencies been cured" and "no allegations that the FDA would not have approved Avastin for particular indications." A18-19 (Op.).

The court also rejected relator's argument that some reimbursement claims were false because treatment with Avastin was not "reasonable and necessary" in those cases. A12 (Op.). The court reasoned that "[t]he central question is . . . whether the 'reasonable and necessary' limitation . . . is a determination made by the relevant administrative agencies or individual doctors." A13 (Op.). The court concluded that CMS, rather than individual doctors, determines whether a treatment is "reasonable and necessary." A16-17 (Op.). Moreover, the court held, an indication that is "medically accepted" is by definition "reasonable and necessary." A14 (Op.). Avastin was "medically accepted" under this definition because it was approved by

FDA for the uses at issue, and it was therefore "reasonable and necessary" as a matter of law. *Id.*; *see* 42 U.S.C. § 1395x(t)(2)(B). The court accordingly held that the amended complaint did "not allege any facts to show that CMS would find Avastin not to be medically reasonable and necessary for any particular use in the but-for world." A17 (Op.). "Avastin would have legally still been reasonable and necessary for the uses at issue" even if Petratos's allegations were true. *Id.* As a result, Petratos "ha[d] not alleged any false claim based on the 'reasonable and necessary' requirement." *Id.*

SUMMARY OF ARGUMENT

The district court's opinion raises significant questions regarding the criteria for Medicare and Medicaid reimbursement and the circumstances under which false or fraudulent statements to FDA and physicians can lead to False Claims Act liability.

Although the district court correctly recognized that CMS has the ultimate authority to determine whether an item or service is "reasonable and necessary," the court erred by reducing that inquiry to whether a drug is prescribed for a "medically accepted" indication. Medicare rules identify

other factors relevant to the "reasonable and necessary" determination, including whether the treatment is appropriate for the individual patient based on individual circumstances and generally accepted medical standards. A drug treatment is not per se "reasonable and necessary" because it was prescribed for an FDA-approved indication.

The district court correctly held that violations of FDA adverse-event-reporting requirements can lead to False Claims Act liability. A mere lack of compliance with FDA regulations does not violate the False Claims Act because compliance generally is not a condition of payment under Medicare or Medicaid. However, if FDA would have revoked approval for a drug had it known the truth—a circumstance likely to occur only in rare cases—later claims for reimbursement may provide a basis for False Claims Act liability. A claim can be "false or fraudulent" under the False Claims Act if the defendant obtained access to the government benefit through an antecedent fraud. That circumstance would arise if, for example, a manufacturer's false or misleading statements to FDA caused the agency to not revoke a drug's approval, thereby allowing the drug to remain eligible

for reimbursement by federal health care programs. In such a case, subsequent claims for reimbursement for that drug may be "false or fraudulent" under the FCA.

Finally, the district court erred in concluding that defendants cannot be liable for fraud that induces physicians to prescribe drug treatments paid for by the United States. Physicians play an essential role in the reimbursement process for Medicare and Medicaid. A physician's prescription is generally a prerequisite to reimbursement for drug treatments and, in some cases, the prescribing physician must expressly certify the treatment's medical necessity. Fraud that corrupts this process by inducing physicians to perform these steps when they would not do so otherwise is actionable under the False Claims Act. Under Supreme Court and Third Circuit precedent, a defendant can be liable for fraudulent efforts to obtain government money even if the fraud was directed in the first instance at a third party integral to the payment process, rather than at the United States. Fraud directed at physicians in the first instance may

therefore establish FCA liability if government reimbursement was a reasonably foreseeable result.

ARGUMENT

I. THE "REASONABLE AND NECESSARY" REQUIREMENT IS NOT COTERMINOUS WITH FDA APPROVAL OR LISTING IN THIRD-PARTY COMPENDIA

The district court correctly recognized that CMS (or its administrative contractors) is ultimately responsible for determining whether a treatment is "reasonable and necessary for the diagnosis or treatment of illness or injury." 42 U.S.C. § 1395y(a)(1)(A); A16-17 (Op.).[7] The court erred, however, by failing to recognize that the "reasonable and necessary"

[7] *See* 42 U.S.C. §§ 1395y(l), 1395ff(a), (f); *see also, e.g.*, *id.* § 1395ff(c)(3)(B) (discussing initial determination and reconsideration by administrative contractor of whether treatment is "reasonable and necessary"); *Heckler v. Ringer*, 466 U.S. 602, 617 (1984) ("The Secretary's decision as to whether a particular medical service is 'reasonable and necessary' and the means by which she implements her decision . . . are clearly discretionary decisions."); *New York ex rel. Bodnar v. Secretary of Health & Human Servs.*, 903 F.2d 122, 125 (2d Cir. 1990) ("The Medicare statute unambiguously vests final authority in the Secretary, and no one else, to determine whether a service is reasonable and necessary, and thus whether reimbursement should be made.").

determination extends beyond merely ascertaining whether a drug is prescribed for an approved use.

The district court held that a drug prescribed for a "medically accepted indication"—that is, one "approved by the FDA or supported by [specific] compendia"—is by definition "reasonable and necessary." A14 (Op.) (quoting *United States ex rel. Simpson v. Bayer Corp.*, No. 05-3895, 2013 WL 4710587, at *11 (D.N.J. Aug. 30, 2013)); 42 U.S.C. § 1395x(t)(2)(A) (defining the term "drug" to include chemotherapy drugs used for a "medically accepted indication"). The court stated that "the 'reasonable and necessary' standard [is] coterminous with the 'medically accepted' requirement." A14 (Op.). The court therefore concluded that Petratos could not concede that "'Avastin is approved by the FDA and supported by compendia listings'" and "'still argue that prescriptions [for] Avastin were not reasonable and necessary.'" A14 (Op.) (alteration in original).

This reading misunderstands the statute. As explained above, *see supra* pp. 9-10 & n.4, CMS may determine that a drug treatment is not "reasonable and necessary" even if it is prescribed for an FDA-approved

use. *Cf. Almy v. Sebelius*, 679 F.3d 297, 308 (4th Cir. 2012) ("While FDA approval [for a medical device] may . . . inform the Secretary's decision as to whether a device is 'reasonable and necessary,' it cannot tie the Secretary's hands."). In addition to FDA approval, the treatment must also be "reasonable and necessary *for [the] individual patient*" based on both "accepted standards of medical practice and the medical circumstances of the individual case." *See* Medicare Benefit Policy Manual, ch. 15, § 50.4.3 (emphasis added). CMS guidance provides examples of when a drug use is not "reasonable and necessary." *Id.* For example, a drug use is not "reasonable and necessary" for Medicare Part B if standard medical practice indicates that oral administration (as opposed to injection) "is effective and is an accepted or preferred method of administration," or if the administration of injections "exceed[s] the frequency or duration of injections indicated by accepted standards of medical practice." *Id.*

The district court's contrary conclusion would unduly limit CMS in executing its statutory authority to review whether an item or service is reasonable and necessary. It also incorrectly implies that False Claims Act

liability may never attach so long as a drug is prescribed for an FDA-approved use (or one supported by the relevant compendia). This Court should accordingly clarify that the "reasonable and necessary" requirement is broader than, and not coterminous with, whether a drug treatment is prescribed for a "medically accepted" use.

II. FAILURE TO REPORT ADVERSE EVENTS MAY IN RARE CASES CREATE FALSE CLAIMS ACT LIABILITY

The district court correctly recognized that violations of FDA adverse-event-reporting requirements can lead to False Claims Act liability. The court explained that non-compliance with regulations can form the basis for an FCA violation if the plaintiff can show that "if the Government had been aware of the defendant's violations . . . , it would not have paid the defendant's claims." A11 (Op.) (quoting *United States ex rel. Wilkins v. United Health Grp., Inc.*, 659 F.3d 295, 307 (3d Cir. 2011)). The district court ultimately concluded, however, that the relator failed to state a claim under the False Claims Act because "[t]here are no allegations that the FDA would not have approved Avastin for particular indications" absent the alleged misconduct. A18-19 (Op.). The United States agrees that in rare

circumstances, adverse-event-reporting violations may be material to the government's decision to pay claims, thus triggering potential FCA liability.

A. The Supreme Court has held that the False Claims Act—which reaches claims that are "false or fraudulent"—"indicate[s] a purpose to reach any person who knowingly assisted in causing the government to pay claims which were grounded in fraud, without regard to whether that person had direct contractual relations with the government." *United States ex rel. Marcus v. Hess*, 317 U.S. 537, 544-45 (1943). This Court has likewise concluded that FCA liability attaches if a defendant "knowingly assisted in causing the government to pay claims which were grounded in fraud." *United States ex rel. Schmidt v. Zimmer, Inc.*, 386 F.3d 235, 243 (3d Cir. 2004).

A claim can therefore be "false or fraudulent" for purposes of the FCA if it is submitted under a "contract or extension of government benefit [that] was originally obtained through false statements or fraudulent conduct." *United States ex rel. Hendow v. University of Phx.*, 461 F.3d 1166, 1173 (9th Cir. 2006). In that situation, the "subsequent claims are false

because of an original fraud." *Id.* Under this well-established theory—sometimes referred to as "fraud in the inducement," *see id.*—a claim can be "false or fraudulent" even if the specific claim for payment was not facially false and contained no false certification. *See United States v. Veneziale*, 268 F.2d 504, 506 (3d Cir. 1959) (FCA liability may attach where the government has "been compelled to pay an innocent third person as a result of the defendant's fraud in inducing the undertaking"); *see also Hooper v. Lockheed Martin Corp.*, 688 F.3d 1037, 1048-49 (9th Cir. 2012); *In re Baycol Prods. Litig.*, 732 F.3d 869, 876 (8th Cir. 2013); *United States ex rel. Laird v. Lockheed Martin Eng'g & Sci. Servs. Co.*, 491 F.3d 254, 259 (5th Cir. 2007); *Harrison v. Westinghouse Savannah River Co.*, 176 F.3d 776, 787-88 (4th Cir. 1999).

This theory is consistent with Congress's intention "to reach all types of fraud, without qualification, that might result in financial loss to the Government." *United States v. Neifert-White Co.*, 390 U.S. 228, 232 (1968). The FCA's legislative history explains, for example, that a claim "submitted under a contract, loan guarantee, or other agreement which was originally

obtained by means of false statements or other corrupt or fraudulent conduct . . . constitutes a false claim." S. Rep. No. 99-345, at 9. Similarly, "claims may be false even though the services are provided as claimed if, for example, the claimant is ineligible to participate in the program" providing payment. *Id.*

B. Consistent with this theory, it is possible to articulate a viable FCA claim based on materially false or fraudulent statements made to FDA related to drug approval. As explained above, government health programs typically will not pay for a drug unless the drug has first been approved by FDA. Accordingly, if a manufacturer makes false statements to FDA about its drug, and those false statements actually cause FDA to approve the drug application or decline to revoke that approval (*i.e.*, where FDA would not have taken those actions had it known the truth), then FCA liability could potentially attach. That is, liability is possible if the defendant's fraud actually induced FDA to allow the drugs on, or to stay on, the market, rendering them eligible for subsequent reimbursement or payment by the government. *See United States ex rel. Krahling v. Merck &*

Co., 44 F. Supp. 3d 581, 593 (E.D. Pa. 2014) (recognizing viability of fraud-on-FDA theory).[8]

Payment under government health programs is not generally conditioned on a manufacturer's compliance with various FDA procedures, or its compliance with the Federal Food, Drug, and Cosmetic Act. Accordingly, merely demonstrating lack of compliance with those procedures or with that statute is insufficient to establish FCA liability. But in the (rare) circumstances in which the defendant's false statements masked problems that were so serious that FDA would have (for example) withheld or withdrawn its approval of the drug application for all indications had it known the truth, subsequent claims for reimbursement for that drug could be rendered "false or fraudulent" because the government would not have paid for the drugs but for the defendant's

[8] It is irrelevant for this purpose that a false statement is made to FDA rather than CMS (both of which are part of the Department of Health and Human Services). Where "a false statement is integral to a causal chain leading to payment, it is irrelevant how the federal bureaucracy has apportioned the statements among layers of paperwork." *United States ex rel. Main v. Oakland City Univ.*, 426 F.3d 914, 916 (7th Cir. 2005); *Hendow*, 461 F.3d at 1174 (same).

fraud. *See also Wilkins*, 659 F.3d at 307 ("[The] plaintiff must show that if the Government had been aware of the defendant's violations . . . it would not have paid the defendant's claims.").[9]

The United States does not contend that a claim is necessarily false or fraudulent because an antecedent fraud was a "but for" cause of the claim being submitted. At some point the causal chain can become so attenuated that the subsequent claim for payment no longer retains the "taint," *Hess*, 317 U.S. at 543, of the defendant's initial fraud. *Accord Hendow*, 461 F.3d at 1174 (discussing situations where the false statement is "*integral* to a causal chain leading to payment" (emphasis added)); *cf. Paroline v. United States*, 134 S. Ct. 1710, 1720 (2014) (explaining that "[p]roximate cause is a standard aspect of causation in . . . the law of torts"). But the necessary connection between the fraud and the later claim would certainly exist at least in those cases when the effect of the fraud on FDA—enabling the

[9] There may also be other circumstances in which a defendant's fraud causes FDA to take actions that make various claims eligible for reimbursement when they would otherwise have been ineligible. This brief does not attempt to provide an exhaustive catalog of viable theories of FCA liability.

defendant's drugs to qualify or remain qualified for government payment—was a foreseeable and intended reason for the defendant's conduct.

The United States takes no position on whether the relator's complaint states a claim under the theory articulated above. But the Court should not disturb the district court's conclusion that such a theory is potentially viable.

III. FRAUD INTENDED TO INDUCE PHYSICIANS TO PRESCRIBE DRUGS PAID FOR BY THE UNITED STATES MAY CREATE FALSE CLAIMS ACT LIABILITY

The district court erred in concluding that a defendant can never be subject to False Claims Act liability for making false statements that induce a physician to prescribe a drug treatment paid for by the United States. The court reasoned that physicians' actions are irrelevant because the "reasonable and necessary" requirement is both determined by CMS and "coterminous" with FDA approval or compendia support. A16 (Op.). The court therefore concluded that an allegation that a "doctor[] would not have prescribed Avastin" absent the alleged fraud cannot state a claim

under the False Claims Act, so long as the drug was prescribed for a "medically accepted" indication. A17 (Op.).

A. The district court erred by ignoring the essential role physicians play in the reimbursement process. *Goodman v. Sullivan*, 891 F.2d 449, 450 (2d Cir. 1989) ("Congress intend[ed] the physician to be a key figure in determining what services are needed and consequently reimbursable."). Although the court correctly held that CMS has ultimate authority to decide whether a treatment is "reasonable and necessary," it failed to recognize that a physician's determination of medical necessity is a prerequisite to such a finding. As previously discussed, *see supra* pp. 6-7 & 10 n.4, Medicare and Medicaid generally reimburse for a drug use only if it is prescribed by a physician or other qualified medical provider. In some cases, Medicare and Medicaid further require that the physician certify the treatment's medical necessity. For example, to obtain Medicare Part B reimbursement for outpatient drugs administered in a physician's office—as is often the case for Avastin—the physician must submit a reimbursement form bearing the express certification that the treatment

was "medically necessary and personally furnished by me or . . . my employee under my direct supervision." CMS Form 1500.

B. Because physician action is an essential prerequisite to reimbursement, fraud intended to induce a provider to perform these steps when the provider would not have done so otherwise may be actionable under the False Claims Act. In such a case, the fraud would be "an important, even an essential factor in subjecting the government to an enforceable demand for money." *Veneziale*, 268 F.2d at 505. Liability may therefore attach because the perpetrator "caus[ed] the government to pay claims which were grounded in fraud," regardless of whether "that person had direct contractual relations with the government." *Hess*, 317 U.S. at 544.

The Supreme Court's decision in *Hess* is instructive. In *Hess*, the defendants submitted collusive bids to local governments for various projects. The bidders were aware that these projects were partly funded by the federal government, but they lacked any direct contractual relationship with the United States. *Hess*, 317 U.S. at 542-43. The Supreme Court

nonetheless concluded that the bidders were subject to False Claims Act liability because their fraudulent conduct "caused the [United States] to pay claims of the local sponsors in order that they might in turn pay [the defendants] under contracts found to have been executed as the result of the fraudulent bidding." *Id.* at 543. "The initial fraudulent action and every step thereafter taken, pressed ever to the ultimate goal—payment of government money to persons who had caused it to be defrauded." *Id.* at 543-44. As a result, the "fraud did not spend itself with the execution of the contract," but rather "taint[ed]" the later claims that caused the United States to reimburse the local governments. *Id.* at 543.

A reimbursement claim may likewise be "fraudulent" if a defendant fraudulently induces a physician to prescribe a drug treatment paid for by Medicare or Medicaid. In such a case, the fraud committed on the physician would not "spend itself" with the physician's decision to prescribe a drug (and, if applicable, submit a reimbursement claim and certify the treatment's medical necessity), but would "taint" the resulting request for reimbursement.

As explained above, the United States does not contend that a claim is necessarily false or fraudulent simply because an antecedent fraud was a "but for" cause of the claim's submission. But liability may attach where the connection between the fraud and the claim is sufficiently close. That would be the case if, for example, a relator could demonstrate that a defendant's fraud was intended to induce physicians to prescribe a drug and it was reasonably foreseeable that the federal government would pay for the treatment. *Cf. In re Neurontin Mktg. & Sales Practices Litig.*, 712 F.3d 21, 39 (1st Cir. 2013) (finding for purposes of RICO claim that fraudulent marketing to doctors was proximate cause of economic loss to private insurer that had to pay for increased prescriptions).

A defendant in such a case cannot escape liability because it directed its fraud in the first instance at a third party integral to the reimbursement process, rather than at the United States. In *Hess*, the Supreme Court held that the False Claims Act applies to fraudulent conduct that causes a third party to submit claims to the United States for amounts higher than would have been submitted otherwise, even absent any false statement to the

United States itself. 317 U.S. at 542-44. This Court in *United States v. Lagerbusch*, 361 F.2d 449, 449 (3d Cir. 1966), likewise held that an employee was liable under the FCA for making false representations to obtain money from his employer, a government contractor reimbursed by the United States. *Lagerbusch* rejected the argument that the False Claims Act did not apply because the false statements were not made to the United States. Citing *Hess*, the Court held that "[w]e have no doubt that the False Claims Act covers such an indirect mulcting of the government." *Lagerbusch*, 361 F.2d at 449. The Senate Judiciary Committee later endorsed *Lagerbusch* in the legislative history of the 1986 amendments to the False Claims Act, explaining that "a false claim is actionable although the claims or false statements were made to a party other than the Government, if the payment thereon would ultimately result in a loss to the United States." S. Rep. No. 99-345, at 10.

The United States takes no position on whether the relator has adequately alleged a False Claims Act violation under this theory. But the

Court should not endorse the district court's holding that suits under this theory can never be viable.

CONCLUSION

For the foregoing reasons, the Court's decision in this case should reflect that (1) Medicare's "reasonable and necessary" requirement is not coterminous with whether a drug is prescribed for a "medically accepted" use; (2) violations of FDA adverse-event-reporting regulations can in rare instances create FCA liability; and (3) FCA liability may attach in some cases if a defendant fraudulently induces a physician to prescribe a drug treatment paid for by the United States.

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MAY 2016

REQUIRED CERTIFICATIONS

I hereby certify that:

1. This brief complies with the requirements of Fed. R. App. P. 32(a)(5) and (6) because it has been prepared in 14-point Palatino Linotype, a proportionally spaced font.

This brief complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B) because it contains **6,069 words**, excluding the parts of the brief exempted under Rule 32(a)(7)(B)(iii) and this Court's local rules, according to the count of Microsoft Word.

2. The text of the electronic copy of the brief is identical to the text in the paper copies.

3. The electronic brief was scanned for viruses using Symantec Endpoint Protection 12.1.6 and no virus was detected.

4. Undersigned counsel is a federal government attorney and is not required to be a member of the Bar of this Court.

s/ Weili J. Shaw
WEILI J. SHAW

CERTIFICATE OF SERVICE

I hereby certify that on May 23, 2016, I electronically filed the foregoing with the Clerk of the Court using the appellate CM/ECF system. Counsel for all parties to the case are registered CM/ECF users and will be served by the CM/ECF system.

s/ Weili J. Shaw
WEILI J. SHAW

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31 U.S.C. § 3729

§ 3729. False claims

(a) LIABILITY FOR CERTAIN ACTS.—

(1) In general.—Subject to paragraph (2), any person who—

(A) knowingly presents, or causes to be presented, a false or fraudulent claim for payment or approval;

(B) knowingly makes, uses, or causes to be made or used, a false record or statement material to a false or fraudulent claim;

. . . .

is liable to the United States Government for a civil penalty of not less than $5,000 and not more than $10,000, as adjusted by the Federal Civil Penalties Inflation Adjustment Act of 1990 (28 U.S.C. 2461 note; Public Law 104-4101[1]), plus 3 times the amount of damages which the Government sustains because of the act of that person.

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[1] So in original. Probably should be "101-410".

42 U.S.C. § 1395x

§ 1395x. Definitions

. . . .

(t) Drugs and biologicals

(1) The term "drugs" and the term "biologicals", except for purposes of subsection (m)(5) of this section and paragraph (2) include only such drugs (including contrast agents) and biologicals, respectively, as are included (or approved for inclusion) in the United States Pharmacopoeia, the National Formulary, or the United States Homeopathic Pharmacopoeia, or in New Drugs or Accepted Dental Remedies (except for any drugs and biologicals

unfavorably evaluated therein), or as are approved by the pharmacy and drug therapeutics committee (or equivalent committee) of the medical staff of the hospital furnishing such drugs and biologicals for use in such hospital.

(2)(A) For purposes of paragraph (1), the term "drugs" also includes any drugs or biologicals used in an anticancer chemotherapeutic regimen for a medically accepted indication (as described in subparagraph (B)).

(B) In subparagraph (A), the term "medically accepted indication", with respect to the use of a drug, includes any use which has been approved by the Food and Drug Administration for the drug, and includes another use of the drug if—

(i) the drug has been approved by the Food and Drug Administration; and

(ii)(I) such use is supported by one or more citations which are included (or approved for inclusion) in one or more of the following compendia: the American Hospital Formulary Service-Drug Information, the American Medical Association Drug Evaluations, the United States Pharmacopoeia-Drug Information (or its successor publications), and other authoritative compendia as identified by the Secretary, unless the Secretary has determined that the use is not medically appropriate or the use is identified as not indicated in one or more such compendia, or

(II) the carrier involved determines, based upon guidance provided by the Secretary to carriers for determining accepted uses of drugs, that such use is medically accepted based on supportive clinical evidence in peer reviewed medical literature appearing in publications which have been identified for purposes of this subclause by the Secretary.

The Secretary may revise the list of compendia in clause (ii)(I) as is appropriate for identifying medically accepted indications for drugs. On and after January 1, 2010, no compendia may be included on the list of compendia under this subparagraph unless the compendia has4 a publicly transparent process for evaluating therapies and for identifying potential conflicts of interests.

. . . .

42 U.S.C. § 1395y

§ 1395y. Exclusions from coverage and medicare as secondary payer

(a) Items or services specifically excluded

Notwithstanding any other provision of this subchapter, no payment may be made under part A or part B of this subchapter for any expenses incurred for items or services—

(1)(A) which, except for items and services described in a succeeding subparagraph or additional preventive services (as described in section 1395x(ddd)(1) of this title), are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member,

. . . .

Medicare Benefit Policy Manual
Chapter 1 - Inpatient Hospital Services Covered Under Part A

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(Rev. 189, 06-27-14)

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Nursing and other related services, use of hospital facilities, and medical social services ordinarily furnished by the hospital for the care and treatment of inpatients are covered under hospital insurance and included in the Prospective Payment system payment.

NOTE: The services of a private-duty nurse or other private-duty attendant are not covered. Private-duty nurses or private-duty attendants are registered nurses, licensed practical nurses, or any other trained attendant whose services ordinarily are rendered to, and restricted to, a particular patient by arrangement between the patient and the private-duty nurse or attendant. Such persons are engaged or paid by an individual patient or by someone acting on their behalf, including a hospital that initially incurs the costs and looks to the patient for reimbursement for such noncovered services.

Where the hospital acts on behalf of a patient, the services of the private-duty nurse or other attendant under such an arrangement are not inpatient hospital services regardless of the control which the hospital may exercise with respect to the services rendered by such private-duty nurse or attendant.

20.1 - Anesthetist Services

(Rev. 1, 10-01-03)
A3-3101.2.A, HO-210.2.A

If the hospital engages the services of a nurse anesthetist or other nonphysician anesthetist (either on a salary or fee-for-service basis) under arrangements which provide for billing to be made by the hospital, the cost of the service when provided to an inpatient could be covered under Part A. (See the Medicare Claims Processing Manual for more information.)

20.2 - Medical Social Services to Meet the Patient's Medically Related Social Needs

(Rev. 1, 10-01-03)
A3-3101.2.B, HO-210.2.B

Medical social services are services which contribute meaningfully to the treatment of a patient's condition. Such services include, but are not limited to:

- Assessment of the social and emotional factors related to the patient's illness, need for care, response to treatment, and adjustment to care in the facility;
- Appropriate action to obtain case work services to assist in resolving problems in these areas; and
- Assessment of the relationship of the patient's medical and nursing requirements to their home situation, financial resources, and the community resources available to them in making the decision regarding their discharge.

30 - Drugs and Biologicals

(Rev. 1, 10-01-03)
A3-3101.3, HO-210.3

Drugs and biologicals for use in the hospital, which are ordinarily furnished by the hospital for the care and treatment of inpatients, are covered.

Three basic requirements must be met for a drug or biological furnished by a hospital to be a covered hospital service:

1. The drug or biological must represent a cost to the institution in rendering services to the beneficiary;

2. The drug or biological must meet the statutory definition. Under the statute, payment may be made for a drug or biological only where it is included, or approved for inclusion, in the latest official edition of the United States Pharmacopoeia-National Formulary (USP-NF), the United States Pharmacopoeia Drug Information (USP DI), or the American Dental Association (ADA) Guide to Dental Therapeutics, except for those drugs and biologicals unfavorably evaluated in the ADA Guide to Dental Therapeutics. Combination drugs are also included in the definition of drugs if the combination itself or all of the therapeutic ingredients of the combination are included, or approved for inclusion, in any of the above drug compendia. Drugs and biologicals are considered approved for inclusion in a compendium if approved under the established procedure by the professional organization responsible for revision of the compendium; or be approved by the pharmacy and drug therapeutics or equivalent committee of the medical staff of the hospital for use in the hospital; and

3. Use of the drug or biological must be safe and effective and otherwise reasonable and necessary as specified in the Medicare Benefit Policy Manual, Chapter 15, "Covered Medical and Other Health Services," §50.

   Drugs or biologicals approved for marketing by the Food and Drug Administration (FDA) are considered safe and effective for purposes of this last requirement when used for indications specified in the labeling. Therefore, use of an FDA-approved drug or biological is covered if:

   - It was administered on or after the date of the FDA's approval;
   - It is reasonable and necessary for the individual patient; and
   - All other applicable coverage requirements are met.

Drugs and biologicals, which have not received final marketing approval by the FDA, are not covered unless CMS instructs the intermediary to the contrary. However, FDA-approved drugs are used for indications other than those specified on the labeling. As long as the FDA has not specified such use as nonapproved, coverage is determined

taking into consideration the generally accepted medical practice in the community. For example, the labeling of certain chemotherapeutic drugs indicates their use in the therapy of specified types of cancer. However, based on experience and empirical evidence, physicians may prescribe these drugs for a wider range of cancer treatments than what is indicated in the labeling. Local medical review policy may or may not grant coverage, depending on the circumstances.

Determinations as to whether use of a drug or biological is reasonable and necessary for an individual patient are the responsibility of the Quality Improvement Organization (QIO), if this is part of the review for a PPS acute care admission. However, if this is an excluded service claim being reviewed by the intermediary, the intermediary reviews and makes a determination, unless it cannot and needs to refer it to the QIO for an initial determination.

A hospital stay solely for the purpose of use of a drug or biological that is determined not reasonable and necessary is not covered.

30.1 - Drugs Included in the Drug Compendia

(Rev. 1, 10-01-03)
A3-3101.2.A, HO-210.3.A

Medicare covers only those drugs and biologicals included, or approved for inclusion, in the latest official edition or revision of the compendia as previously listed.

Where a drug is excluded from coverage because it is unfavorably evaluated in either the AMA Drug Evaluations or Accepted Dental Therapeutics, the exclusion applies to all uses for which the drug or biological was so unfavorably evaluated.

Drugs and biologicals are considered "approved for inclusion" in a compendium if approved under the procedure established by the professional organization responsible for revision of the compendium.

30.2 - Approval by Pharmacy and Drug Therapeutics Committee

(Rev. 1, 10-01-03)
A3-3101.3.B, HO-210.3.B

A pharmacy and drug therapeutics or equivalent committee is a medical staff committee that confers with the hospital pharmacist in the formulation of policies pertaining to drugs. Drugs and biologicals approved for use in the hospital by such a committee are covered only if the committee develops and maintains a formulary or list of drugs accepted for use in the hospital. The committee need not function exclusively as a pharmacy and drug therapeutics committee but may also carry on other medical staff functions.

Drugs and biologicals are considered approved for use in the hospital if selected for inclusion in the hospital drug list of formulary under the procedure of the committee

established for that purpose. Express approval is required; the fact that a drug or biological has not been specifically determined to be unacceptable for use in the hospital does not constitute approval.

Drugs and biologicals are covered if approved for general use in the hospital, or if approved for use by a particular patient or group of patients. Approval by a pharmacy and drug therapeutics committee is an alternative to approval for inclusion of the drug or biological in an approved drug compendium (see §30.1 above); such approval does not preclude the need for a determination of medical necessity. An investigational drug is not considered to meet the reasonable and necessary test since its efficacy has not yet been established.

The decision of individual hospitals should not transcend the determinations of the Food and Drug Administration and Public Health Service in respect to the safety and effectiveness of drugs. Therefore, even if approved by an appropriate hospital committee, the reasonable cost of an investigational or other nonapproved drug or biological (e.g., Laetrile) cannot be reimbursed. This exclusion from payment applies whether or not the drug or biological is administered during the course of an otherwise covered hospital stay, since payment may not be made for items and services that are not reasonable and necessary. A hospital stay solely for the purpose of administering a drug or biological that is not reasonable and necessary, including an investigational drug or biological, is not covered and the drug or biological itself is not covered.

30.3 - Combination Drugs

(Rev. 1, 10-01-03)
A3-3101.3.C, HO-210-3.C

Combination drugs are covered if the combination itself or all of the therapeutic ingredients of the combination are included, or approved for inclusion, in any of the designated drug compendia. **Any** combination drug approved for use in the hospital by the pharmacy and drug therapeutics or equivalent committee is covered.

30.4 - Drugs Specially Ordered for Inpatients

(Rev. 1, 10-01-03)
A3-3101.3.D, HO-210.3.D

Coverage is not limited to drugs and biologicals routinely stocked by the hospital; a drug or biological not stocked by the hospital, which the hospital obtains for the patient from an outside source, such as a community pharmacy, can also be covered.

Drugs and biologicals not included in the drug list or formulary maintained by the hospital's pharmacy and drug therapeutics committee may be covered if the hospital has a policy which permits such drugs to be furnished to a patient at the special request of a physician. However, in order to be covered, such drugs and biologicals must be included, or approved for inclusion, in one of the designated drug compendia. (In addition, a

combination drug, or all of its therapeutic ingredients, would have to be included or approved for inclusion in one of the compendia.)

30.5 - Drugs for Use Outside the Hospital

(Rev. 1, 10-01-03)
A3-3101.3.E, HO-210.3.E

Drugs and biologicals furnished by a hospital to an inpatient for use outside the hospital are, in general, not covered as inpatient hospital services. However, if the drug or biological is deemed medically necessary to permit or facilitate the patient's departure from the hospital, and a limited supply is required until the patient can obtain a continuing supply, the limited supply of the drug or biological is covered as an inpatient hospital service.

40 - Supplies, Appliances, and Equipment

(Rev. 1, 10-01-03)
A3-3101.4, HO-210.4

Supplies, appliances, and equipment, which are ordinarily furnished by the hospital for the care and treatment of the beneficiary solely during the inpatient hospital stay, are covered inpatient hospital services.

Under certain circumstances, supplies, appliances, and equipment used during the beneficiary's inpatient stay are covered under Part A even though the supplies, appliances and equipment leave the hospital with the patient upon discharge. These are circumstances in which it would be unreasonable or impossible from a medical standpoint to limit the patient's use of the item to the periods during which the individual is an inpatient. Examples of items covered under this rule are:

- Items permanently installed in or attached to the patient's body while an inpatient, such as cardiac valves, cardiac pacemakers, and artificial limbs; and

- Items which are temporarily installed in or attached to the patient's body while an inpatient, and which are also necessary to permit or facilitate the patient's release from the hospital, such as tracheotomy or drainage tubes.

Hospital “admission packs” containing primarily toilet articles, such as soap, toothbrushes, toothpaste, and combs, are covered under Part A if routinely furnished by the hospital to all its inpatients. If not routinely furnished to all patients, the packs are not covered. In that situation, the hospital may charge beneficiaries for the pack, but only if they request it with knowledge of what they are requesting and what the charge to them will be.

Supplies, appliances, and equipment furnished to an inpatient for use **only** outside the hospital are not, in general, covered as inpatient hospital services. However, a temporary or disposable item, which is medically necessary to permit or facilitate the patient's

Medicare Benefit Policy Manual

Chapter 15 – Covered Medical and Other Health Services

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(Rev. 221, 03-11-16)

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40 - Effect of Beneficiary Agreements Not to Use Medicare Coverage

- 40.1 - Private Contracts Between Beneficiaries and Physicians/Practitioners
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The report is due in CROWD 30 days after the end of each quarter (e.g., a report for the quarter April1, 2010, through June 30, 2010, is due July 30, 2010.)

50 - Drugs and Biologicals

(Rev. 1, 10-01-03)
B3-2049, A3-3112.4.B, HO-230.4.B

The Medicare program provides limited benefits for outpatient drugs. The program covers drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them.

Generally, drugs and biologicals are covered only if all of the following requirements are met:

- They meet the definition of drugs or biologicals (see §50.1);
- They are of the type that are not usually self-administered. (see §50.2);
- They meet all the general requirements for coverage of items as incident to a physician's services (see §§50.1 and 50.3);
- They are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice (see §50.4);
- They are not excluded as noncovered immunizations (see §50.4.4.2); and
- They have not been determined by the FDA to be less than effective. (See §§50.4.4).

Medicare Part B does generally not cover drugs that can be self-administered, such as those in pill form, or are used for self-injection. However, the statute provides for the coverage of some self-administered drugs. Examples of self-administered drugs that are covered include blood-clotting factors, drugs used in immunosuppressive therapy, erythropoietin for dialysis patients, osteoporosis drugs for certain homebound patients, and certain oral cancer drugs. (See §110.3 for coverage of drugs, which are necessary to the effective use of Durable Medical Equipment (DME) or prosthetic devices.)

50.1 - Definition of Drug or Biological

(Rev. 1, 10-01-03)
B3-2049.1

Drugs and biologicals must be determined to meet the statutory definition. Under the statute §1861(t)(1), payment may be made for a drug or biological only where it is included, or approved for inclusion, in the latest official edition of the United States Pharmacopoeia National Formulary (USP-NF), the United States Pharmacopoeia-Drug

Information (USD-DI), or the American Dental Association (AOA) Guide to Dental Therapeutics, except for those drugs and biologicals unfavorably evaluated in the ADA Guide to Dental Therapeutics. The inclusion of an item in the USP DI does not necessarily mean that the item is a drug or biological. The USP DI is a database of drug information developed by the U.S. Pharmacopoeia but maintained by Micromedex, which contains medically accepted uses for generic and brand name drug products. Inclusion in such reference (or approval by a hospital committee) is a necessary condition for a product to be considered a drug or biological under the Medicare program, however, it is not enough. Rather, the product must also meet all other program requirements to be determined to be a drug or biological. Combination drugs are also included in the definition of drugs if the combination itself or all of the therapeutic ingredients of the combination are included, or approved for inclusion, in any of the above drug compendia.

Drugs and biologicals are considered approved for inclusion in a compendium if approved under the established procedure by the professional organization responsible for revision of the compendium.

50.2 - Determining Self-Administration of Drug or Biological

(Rev. 157, Issued: 06-08-12, Effective: 07-01-12, Implementation: 07-02-12)

The Medicare program provides limited benefits for outpatient prescription drugs. The program covers drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Section 112 of the Benefits, Improvements & Protection Act of 2000 (BIPA) amended sections 1861(s)(2)(A) and 1861(s)(2)(B) of the Act to redefine this exclusion. The prior statutory language referred to those drugs "which cannot be self-administered." Implementation of the BIPA provision requires interpretation of the phrase "not usually self-administered by the patient".

A. Policy

Fiscal intermediaries, carriers and Medicare Administrative Contractors (MACs) are instructed to follow the instructions below when applying the exclusion for drugs that are usually self-administered by the patient. Each individual contractor must make its own individual determination on each drug. Contractors must continue to apply the policy that not only the drug is medically reasonable and necessary for any individual claim, but also that the route of administration is medically reasonable and necessary. That is, if a drug is available in both oral and injectable forms, the injectable form of the drug must be medically reasonable and necessary as compared to using the oral form.

For certain injectable drugs, it will be apparent due to the nature of the condition(s) for which they are administered or the usual course of treatment for those conditions, they are, or are not, usually self-administered. For example, an injectable drug used to treat migraine headaches is usually self-administered. On the other hand, an injectable drug, administered at the same time as chemotherapy, used to treat anemia secondary to chemotherapy is not usually self-administered.

B. Administered

The term "administered" refers only to the physical process by which the drug enters the patient's body. It does not refer to whether the process is supervised by a medical professional (for example, to observe proper technique or side-effects of the drug). Injectable drugs, including intravenously administered drugs, are typically eligible for inclusion under the "incident to" benefit. With limited exceptions, other routes of administration including, but not limited to, oral drugs, suppositories, topical medications are considered to be usually self-administered by the patient.

C. Usually

For the purposes of applying this exclusion, the term "usually" means more than 50 percent of the time for all Medicare beneficiaries who use the drug. Therefore, if a drug is self-administered by more than 50 percent of Medicare beneficiaries, the drug is excluded from coverage and the contractor may not make any Medicare payment for it. In arriving at a single determination as to whether a drug is usually self-administered, contractors should make a separate determination for each indication for a drug as to whether that drug is usually self-administered.

After determining whether a drug is usually self-administered for each indication, contractors should determine the relative contribution of each indication to total use of the drug (i.e., weighted average) in order to make an overall determination as to whether the drug is usually self-administered. For example, if a drug has three indications, is not self-administered for the first indication, but is self administered for the second and third indications, and the first indication makes up 40 percent of total usage, the second indication makes up 30 percent of total usage, and the third indication makes up 30 percent of total usage, then the drug would be considered usually self-administered.

Reliable statistical information on the extent of self-administration by the patient may not always be available. Consequently, CMS offers the following guidance for each contractor's consideration in making this determination in the absence of such data:

1. Absent evidence to the contrary, presume that drugs delivered intravenously are not usually self-administered by the patient.

2. Absent evidence to the contrary, presume that drugs delivered by intramuscular injection are not usually self-administered by the patient. (Avonex, for example, is delivered by intramuscular injection, not usually self-administered by the patient.) The contractor may consider the depth and nature of the particular intramuscular injection in applying this presumption. In applying this presumption, contractors should examine the use of the particular drug and consider the following factors:

3. Absent evidence to the contrary, presume that drugs delivered by subcutaneous injection are self-administered by the patient. However, contractors should examine the use of the particular drug and consider the following factors:

A. **Acute Condition -** Is the condition for which the drug is used an acute condition? If so, it is less likely that a patient would self-administer the drug. If the condition were longer term, it would be more likely that the patient would self-administer the drug.

B. Frequency of Administration - How often is the injection given? For example, if the drug is administered once per month, it is less likely to be self-administered by the patient. However, if it is administered once or more per week, it is likely that the drug is self-administered by the patient.

In some instances, carriers may have provided payment for one or perhaps several doses of a drug that would otherwise not be paid for because the drug is usually self-administered. Carriers may have exercised this discretion for limited coverage, for example, during a brief time when the patient is being trained under the supervision of a physician in the proper technique for self-administration. Medicare will no longer pay for such doses. In addition, contractors may no longer pay for any drug when it is administered on an outpatient emergency basis, if the drug is excluded because it is usually self-administered by the patient.

D. Definition of Acute Condition

For the purposes of determining whether a drug is usually self-administered, an acute condition means a condition that begins over a short time period, is likely to be of short duration and/or the expected course of treatment is for a short, finite interval. A course of treatment consisting of scheduled injections lasting less than 2 weeks, regardless of frequency or route of administration, is considered acute. Evidence to support this may include Food and Drug Administration (FDA) approval language, package inserts, drug compendia, and other information.

E. By the Patient

The term “by the patient” means Medicare beneficiaries as a collective whole. The carrier includes only the patients themselves and not other individuals (that is, spouses, friends, or other care-givers are not considered the patient). The determination is based on whether the drug is self-administered by the patient a majority of the time that the drug is used on an outpatient basis by Medicare beneficiaries for medically necessary indications. The carrier ignores all instances when the drug is administered on an inpatient basis.

The carrier makes this determination on a drug-by-drug basis, not on a beneficiary-by-beneficiary basis. In evaluating whether beneficiaries as a collective whole self-administer, individual beneficiaries who do not have the capacity to self-administer any

drug due to a condition other than the condition for which they are taking the drug in question are not considered. For example, an individual afflicted with paraplegia or advanced dementia would not have the capacity to self-administer any injectable drug, so such individuals would not be included in the population upon which the determination for self-administration by the patient was based. Note that some individuals afflicted with a less severe stage of an otherwise debilitating condition would be included in the population upon which the determination for "self-administered by the patient" was based; for example, an early onset of dementia.

F. Evidentiary Criteria

Contractors are only required to consider the following types of evidence: peer reviewed medical literature, standards of medical practice, evidence-based practice guidelines, FDA approved label, and package inserts. Contractors may also consider other evidence submitted by interested individuals or groups subject to their judgment.

Contractors should also use these evidentiary criteria when reviewing requests for making a determination as to whether a drug is usually self-administered, and requests for reconsideration of a pending or published determination.

Note that prior to August 1, 2002, one of the principal factors used to determine whether a drug was subject to the self-administered exclusion was whether the FDA label contained instructions for self-administration. However, CMS notes that under the new standard, the fact that the FDA label includes instructions for self-administration is not, by itself, a determining factor that a drug is subject to this exclusion.

G. Provider Notice of Noncovered Drugs

Contractors must describe on their Web site the process they will use to determine whether a drug is usually self-administered and thus does not meet the "incident to" benefit category. Contractors must publish a list of the injectable drugs that are subject to the self-administered exclusion on their Web site, including the data and rationale that led to the determination. Contractors will report the workload associated with developing new coverage statements in CAFM 21208.

Contractors must provide notice 45 days prior to the date that these drugs will not be covered. During the 45-day time period, contractors will maintain existing medical review and payment procedures. After the 45-day notice, contractors may deny payment for the drugs subject to the notice.

Contractors must not develop local coverage determinations (LCDs) for this purpose because further elaboration to describe drugs that do not meet the 'incident to' and the 'not usually self-administered' provisions of the statute are unnecessary. Current LCDs based solely on these provisions must be withdrawn. LCDs that address the self-administered exclusion and other information may be reissued absent the self-administered drug exclusion material. Contractors will report this workload in CAFM

21206. However, contractors may continue to use and write LCDs to describe reasonable and necessary uses of drugs that are not usually self-administered.

H. Conferences Between Contractors

Contractors' Medical Directors may meet and discuss whether a drug is usually self-administered without reaching a formal consensus. Each contractor uses its discretion as to whether or not it will participate in such discussions. Each contractor must make its own individual determinations, except that fiscal intermediaries may, at their discretion, follow the determinations of the local carrier with respect to the self-administered exclusion.

I. Beneficiary Appeals

If a beneficiary's claim for a particular drug is denied because the drug is subject to the "self-administered drug" exclusion, the beneficiary may appeal the denial. Because it is a "benefit category" denial and not a denial based on medical necessity, an Advance Beneficiary Notice (ABN) is not required. A "benefit category" denial (i.e., a denial based on the fact that there is no benefit category under which the drug may be covered) does not trigger the financial liability protection provisions of Limitation On Liability (under §1879 of the Act). Therefore, physicians or providers may charge the beneficiary for an excluded drug.

J. Provider and Physician Appeals

A physician accepting assignment may appeal a denial under the provisions found in Pub. 100-04, Medicare Claims Processing Manual, chapter 29.

K. Reasonable and Necessary

Contractors will make the determination of reasonable and necessary with respect to the medical appropriateness of a drug to treat the patient's condition. Contractors will continue to make the determination of whether the intravenous or injection form of a drug is appropriate as opposed to the oral form. Contractors will also continue to make the determination as to whether a physician's office visit was reasonable and necessary. However, contractors should not make a determination of whether it was reasonable and necessary for the patient to choose to have his or her drug administered in the physician's office or outpatient hospital setting. That is, while a physician's office visit may not be reasonable and necessary in a specific situation, in such a case an injection service would be payable.

L. Reporting Requirements

Each carrier, intermediary and Medicare Administrative Contractor (MAC) must report to CMS its complete list of injectable drugs that the contractor has determined are excluded when furnished incident to a physician's service on the basis that the drug is

usually self-administered. The CMS expects that contractors will review injectable drugs on a rolling basis and update their list of excluded drugs as it is developed and no less frequently than annually. For example, contractors should not wait to publish this list until every drug has been reviewed. Contractors must enter their self-administered drug exclusion list to the Medicare Coverage Database (MCD). This database can be accessed at www.cms.hhs.gov/mcd. See Pub.100-08, Medicare Program Integrity Manual, Chapter 3, Section 3.3, "Policies and Guidelines Applied During Review", for instructions on submitting these lists to the MCD.

M. Drugs Treated as Hospital Outpatient Supplies

In certain circumstances, Medicare pays for drugs that may be considered usually self-administered by the patient when such drugs function as supplies. This is the case when the drugs provided are an integral component of a procedure or are directly related to it, i.e., when they facilitate the performance of or recovery from a particular procedure. Except for the applicable copayment, hospitals may not bill beneficiaries for these types of drugs because their costs, as supplies, are packaged into the payment for the procedure with which they are used. Listed below are examples of when drugs are treated as supplies and hospitals should bill Medicare for the drug as a supply and should not separately bill the beneficiary.

- Sedatives administered to a patient while he or she is in the preoperative area being prepared for a procedure.

- Mydriatic drops instilled into the eye to dilate the pupils, anti-inflammatory drops, antibiotic drops/ointments, and ocular hypotensives that are administered to a patient immediately before, during, or immediately following an ophthalmic procedure. This does not refer to the patient's eye drops that the patient uses pre- and postoperatively.

- Barium or low osmolar contrast media provided integral to a diagnostic imaging procedure.

- Topical solution used with photodynamic therapy furnished at the hospital to treat nonhyperkeratotic actinic keratosis lesions of the face or scalp.

- Antibiotic ointments such as bacitracin, placed on a wound or surgical incision at the completion of a procedure.

The following are examples of when a drug is not directly related or integral to a procedure, and does not facilitate the performance of or recovery from a procedure. Therefore the drug is not considered a packaged supply. In many of these cases the drug itself is the treatment instead of being integral or directly related to the procedure, or facilitating the performance of or recovery from a particular procedure.

- Drugs given to a patient for his or her continued use at home after leaving the hospital.

- Oral pain medication given to an outpatient who develops a headache while receiving chemotherapy administration treatment.

- Daily routine insulin or hypertension medication given preoperatively to a patient.

- A fentanyl patch or oral pain medication such as hydrocodone, given to an outpatient presenting with pain.

- A laxative suppository for constipation while the patient waits to receive an unrelated X-ray.

These two lists of examples may serve to guide hospitals in deciding which drugs are supplies packaged as a part of a procedure, and thus may be billed under Part B. Hospitals should follow CMS' guidance for billing drugs that are packaged and paid as supplies, reporting coded and uncoded drugs with their charges under the revenue code associated with the cost center under which the hospital accumulates the costs for the drugs.

50.3 - Incident To Requirements

(Rev. 1, 10-01-03)
B3-2049.3

In order to meet all the general requirements for coverage under the incident-to provision, an FDA approved drug or biological must:

- Be of a form that is not usually self-administered;

- Must be furnished by a physician; and

- Must be administered by the physician, or by auxiliary personnel employed by the physician and under the physician's personal supervision.

The charge, if any, for the drug or biological must be included in the physician's bill, and the cost of the drug or biological must represent an expense to the physician. Drugs and biologicals furnished by other health professionals may also meet these requirements. (See §§170, 180, 190 and 200 for specific instructions.)

Whole blood is a biological, which cannot be self-administered and is covered when furnished incident to a physician's services. Payment may also be made for blood fractions if all coverage requirements are satisfied and the blood deductible has been met.

50.4 - Reasonableness and Necessity

(Rev. 1, 10-01-03)

B3-2049.4

50.4.1 - Approved Use of Drug

(Rev. 1, 10-01-03)
B3-2049.4

Use of the drug or biological must be safe and effective and otherwise reasonable and necessary. (See the Medicare Benefit Policy Manual, Chapter 16, "General Exclusions from Coverage," §20.) Drugs or biologicals approved for marketing by the Food and Drug Administration (FDA) are considered safe and effective for purposes of this requirement when used for indications specified on the labeling. Therefore, the program may pay for the use of an FDA approved drug or biological, if:

- It was injected on or after the date of the FDA's approval;
- It is reasonable and necessary for the individual patient; and
- All other applicable coverage requirements are met.

The carrier, DMERC, or intermediary will deny coverage for drugs and biologicals, which have not received final marketing approval by the FDA unless it receives instructions from CMS to the contrary. For specific guidelines on coverage of Group C cancer drugs, see the Medicare National Coverage Determinations Manual.

If there is reason to question whether the FDA has approved a drug or biological for marketing, the carrier or intermediary must obtain satisfactory evidence of FDA's approval. Acceptable evidence includes:

- A copy of the FDA's letter to the drug's manufacturer approving the new drug application (NDA);
- A listing of the drug or biological in the FDA's "Approved Drug Products" or "FDA Drug and Device Product Approvals";
- A copy of the manufacturer's package insert, approved by the FDA as part of the labeling of the drug, containing its recommended uses and dosage, as well as possible adverse reactions and recommended precautions in using it; or
- Information from the FDA's Web site.

When necessary, the regional office (RO) may be able to help in obtaining information.

50.4.2 - Unlabeled Use of Drug

(Rev. 1, 10-01-03)
B3-2049.3

An unlabeled use of a drug is a use that is not included as an indication on the drug's label as approved by the FDA. FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if the carrier determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice. In the case of drugs used in an anti-cancer chemotherapeutic regimen, unlabeled uses are covered for a medically accepted indication as defined in §50.5.

These decisions are made by the contractor on a case-by-case basis.

50.4.3 - Examples of Not Reasonable and Necessary

(Rev. 1, 10-01-03)
B3-2049.4

Determinations as to whether medication is reasonable and necessary for an individual patient should be made on the same basis as all other such determinations (i.e., with the advice of medical consultants and with reference to accepted standards of medical practice and the medical circumstances of the individual case). The following guidelines identify three categories with specific examples of situations in which medications would not be reasonable and necessary according to accepted standards of medical practice:

1. Not for Particular Illness

Medications given for a purpose other than the treatment of a particular condition, illness, or injury are not covered (except for certain immunizations). Charges for medications, e.g., vitamins, given simply for the general good and welfare of the patient and not as accepted therapies for a particular illness are excluded from coverage.

2. Injection Method Not Indicated

Medication given by injection (parenterally) is not covered if standard medical practice indicates that the administration of the medication by mouth (orally) is effective and is an accepted or preferred method of administration. For example, the accepted standard of medical practice for the treatment of certain diseases is to initiate therapy with parenteral penicillin and to complete therapy with oral penicillin. Carriers exclude the entire charge for penicillin injections given after the initiation of therapy if oral penicillin is indicated unless there are special medical circumstances that justify additional injections.

3. Excessive Medications

Medications administered for treatment of a disease and which exceed the frequency or duration of injections indicated by accepted standards of medical practice are not covered. For example, the accepted standard of medical practice in the maintenance treatment of pernicious anemia is one vitamin B-12 injection per month. Carriers exclude the entire charge for injections given in excess of this frequency unless there are special medical circumstances that justify additional injections.

Carriers will supplement the guidelines as necessary with guidelines concerning appropriate use of specific injections in other situations. They will use the guidelines to screen out questionable cases for special review, further development, or denial when the injection billed for would not be reasonable and necessary. They will coordinate any type of drug treatment review with the Quality Improvement Organization (QIO).

If a medication is determined not to be reasonable and necessary for diagnosis or treatment of an illness or injury according to these guidelines, the carrier excludes the entire charge (i.e., for both the drug and its administration). Also, carriers exclude from payment any charges for other services (such as office visits) which were primarily for the purpose of administering a noncovered injection (i.e., an injection that is not reasonable and necessary for the diagnosis or treatment of an illness or injury).

50.4.4 - Payment for Antigens and Immunizations
(Rev. 1, 10-01-03)

50.4.4.1 - Antigens
(Rev. 186, Issued: 04-16-14, Effective: 01-01 01, Implementation: 05-12-14)

Payment may be made for a reasonable supply of antigens that have been prepared for a particular patient if: (1) the antigens are prepared by a physician who is a doctor of medicine or osteopathy, and (2) the physician who prepared the antigens has examined the patient and has determined a plan of treatment and a dosage regimen.

Antigens must be administered in accordance with the plan of treatment and by a doctor of medicine or osteopathy or by a properly instructed person (who could be the patient) under the supervision of the doctor. The associations of allergists that CMS consulted advised that a reasonable supply of antigens is considered to be not more than a 12-month supply of antigens that has been prepared for a particular patient at any one time. The purpose of the reasonable supply limitation is to assure that the antigens retain their potency and effectiveness over the period in which they are to be administered to the patient. (See §§20.2 and 50.2.)

50.4.4.2 - Immunizations
(Rev. 202, Issued: 12-31-14, Effective: 09-19-14, Implementation: 02-02-15)

Vaccinations or inoculations are excluded as immunizations unless they are directly related to the treatment of an injury or direct exposure to a disease or condition, such as anti-rabies treatment, tetanus antitoxin or booster vaccine, botulin antitoxin, antivenin sera, or immune globulin. In the absence of injury or direct exposure, preventive immunization (vaccination or inoculation) against such diseases as smallpox, polio, diphtheria, etc., is not covered. However, pneumococcal, hepatitis B, and influenza virus vaccines are exceptions to this rule. (See items A, B, and C below.) In cases where a vaccination or inoculation is excluded from coverage, related charges are also not covered.

A. Pneumococcal Pneumonia Vaccinations

1. Background and History of Coverage:

Section 1861(s)(10)(A) of the Social Security Act and regulations at 42 CFR 410.57 authorize Medicare coverage under Part B for pneumococcal vaccine and its administration.

For services furnished on or after May 1, 1981 through September 18, 2014, the Medicare Part B program covered pneumococcal pneumonia vaccine and its administration when furnished in compliance with any applicable State law by any provider of services or any entity or individual with a supplier number. Coverage included an initial vaccine administered only to persons at high risk of serious pneumococcal disease (including all people 65 and older; immunocompetent adults at increased risk of pneumococcal disease or its complications because of chronic illness; and individuals with compromised immune systems), with revaccination administered only to persons at highest risk of serious pneumococcal infection and those likely to have a rapid decline in pneumococcal antibody levels, provided that at least 5 years had passed since the previous dose of pneumococcal vaccine.

Those administering the vaccine did not require the patient to present an immunization record prior to administering the pneumococcal vaccine, nor were they compelled to review the patient's complete medical record if it was not available, relying on the patient's verbal history to determine prior vaccination status.

Effective July 1, 2000, Medicare no longer required for coverage purposes that a doctor of medicine or osteopathy order the vaccine. Therefore, a beneficiary could receive the vaccine upon request without a physician's order and without physician supervision.

2. Coverage Requirements:

Effective for claims with dates of service on and after September 19, 2014, an initial pneumococcal vaccine may be administered to all Medicare beneficiaries who have never received a pneumococcal vaccination under Medicare Part B. A different, second pneumococcal vaccine may be administered 1 year after the first vaccine was administered (i.e., 11 full months have passed following the month in which the last pneumococcal vaccine was administered).

Those administering the vaccine should not require the patient to present an immunization record prior to administering the pneumococcal vaccine, nor should they feel compelled to review the patient's complete medical record if it is not available. Instead, provided that the patient is competent, it is acceptable to rely on the patient's verbal history to determine prior vaccination status.

Medicare does not require for coverage purposes that a doctor of medicine or osteopathy order the vaccine. Therefore, the beneficiary may receive the vaccine upon request without a physician's order and without physician supervision.

B. Hepatitis B Vaccine

Effective for services furnished on or after September 1, 1984, P.L. 98-369 provides coverage under Part B for hepatitis B vaccine and its administration, furnished to a Medicare beneficiary who is at high or intermediate risk of contracting hepatitis B. High-risk groups currently identified include (see exception below):

- ESRD patients;
- Hemophiliacs who receive Factor VIII or IX concentrates;
- Clients of institutions for the mentally retarded;
- Persons who live in the same household as a Hepatitis B Virus (HBV) carrier;
- Homosexual men;
- Illicit injectable drug abusers; and
- Persons diagnosed with diabetes mellitus.

Intermediate risk groups currently identified include:

- Staff in institutions for the mentally retarded; and
- Workers in health care professions who have frequent contact with blood or blood-derived body fluids during routine work.

EXCEPTION: Persons in both of the above-listed groups in paragraph B, would not be considered at high or intermediate risk of contracting hepatitis B, however, if there were laboratory evidence positive for antibodies to hepatitis B. (ESRD patients are routinely tested for hepatitis B antibodies as part of their continuing monitoring and therapy.)

For Medicare program purposes, the vaccine may be administered upon the order of a doctor of medicine or osteopathy, by a doctor of medicine or osteopathy, or by home health agencies, skilled nursing facilities, ESRD facilities, hospital outpatient departments, and persons recognized under the incident to physicians' services provision of law.

A charge separate from the ESRD composite rate will be recognized and paid for administration of the vaccine to ESRD patients.

C. Influenza Virus Vaccine

Effective for services furnished on or after May 1, 1993, the Medicare Part B program covers influenza virus vaccine and its administration when furnished in compliance with any applicable State law by any provider of services or any entity or individual with a supplier number. Typically, these vaccines are administered once a flu season. Medicare does not require, for coverage purposes, that a doctor of medicine or osteopathy order the vaccine. Therefore, the beneficiary may receive the vaccine upon request without a physician's order and without physician supervision.

50.4.5 - Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

(Rev. 212, Issued: 11-06-15, Effective: 08-12-15, Implementation: 02-10-16)

A. Overview

Effective January 1, 1994, off-label, medically accepted indications of Food and Drug Administration-(FDA) approved drugs and biologicals used in an anti-cancer chemotherapeutic regimen are identified under the conditions described below. A regimen is a combination of anti-cancer agents clinically recognized for the treatment of a specific type of cancer. Off-label, medically accepted indications are supported in either one or more of the compendia or in peer-reviewed medical literature. The contractor may maintain its own subscriptions to the listed compendia or peer-reviewed publications to determine the medically accepted indication of drugs or biologicals used off-label in an anti-cancer chemotherapeutic regimen. Compendia documentation or peer-reviewed literature supporting off-label use by the treating physician may also be requested of the physician by the contractor.

B. Recent Revisions to the Compendia List

Do not deny coverage based solely on the absence of FDA-approved labeling for the use, if the use is supported by any of the following compendia and the use is **not** listed as unsupported, not indicated, not recommended, or equivalent terms, in any of the following compendia:

Existing - American Hospital Formulary Service-Drug Information (AHFS-DI)

Effective June 5, 2008 - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium

Effective June 10, 2008 - Micromedex DrugDex

Effective July 2, 2008 - Clinical Pharmacology

Effective August 12, 2015 – Lexi-Drugs

The listed compendia employ various rating and recommendation systems that may not be readily cross-walked from compendium to compendium. In general, a use is identified by a compendium as **medically accepted** if the:

1. indication is a Category 1 or 2A in NCCN, or Class I, Class IIa, or Class IIb in DrugDex; or,

2. narrative text in AHFS-DI or Clinical Pharmacology is supportive, or

3. indication is listed in Lexi-Drugs as "Use: Off-Label" and rated as "Evidence Level A"

A use is **not medically accepted** by a compendium if the:

1. indication is a Category 3 in NCCN or a Class III in DrugDex; or,

2. narrative text in AHFS or Clinical Pharmacology is "not supportive," or

3. indication is listed in Lexi-Drugs as "Use: Unsupported"

The complete absence of narrative text on a use is considered neither supportive nor non-supportive.

C. Use Supported by Clinical Research That Appears in Peer-Reviewed Medical Literature

Contractors may also identify off-label uses that are supported by clinical research under the conditions identified in this section. Peer-reviewed medical literature may appear in scientific, medical, and pharmaceutical publications in which original manuscripts are published, only after having been critically reviewed for scientific accuracy, validity, and reliability by unbiased, independent experts prior to publication. In-house publications of entities whose business relates to the manufacture, sale, or distribution of pharmaceutical products are excluded from consideration. Abstracts (including meeting abstracts) are excluded from consideration.

In determining whether an off-label use is supported, the contractors will evaluate the evidence in published, peer-reviewed medical literature listed below. When evaluating this literature, they will consider (among other things) the following:

- Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence.

- Whether the administered chemotherapy regimen is adequately represented in the published evidence.

- Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients.

- Whether the study is appropriate to address the clinical question. The contractor will consider:

1. whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover.);

2. that non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs; and,

3. that case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

The contractor will use peer-reviewed medical literature appearing in the regular editions of the following publications, not to include supplement editions privately funded by parties with a vested interest in the recommendations of the authors:

American Journal of Medicine;
Annals of Internal Medicine;
Annals of Oncology;
Annals of Surgical Oncology;
Biology of Blood and Marrow Transplantation;
Blood;
Bone Marrow Transplantation;
British Journal of Cancer;
British Journal of Hematology;
British Medical Journal;
Cancer;
Clinical Cancer Research;
Drugs;
European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology);
Gynecologic Oncology;
International Journal of Radiation, Oncology, Biology, and Physics;
The Journal of the American Medical Association;
Journal of Clinical Oncology;
Journal of the National Cancer Institute;
Journal of the National Comprehensive Cancer Network (NCCN);
Journal of Urology;
Lancet;
Lancet Oncology;
Leukemia;
The New England Journal of Medicine; or
Radiation Oncology

D. Generally

FDA-approved drugs and biologicals may also be considered for use in the determination of medically accepted indications for off-label use if determined by the contractor to be reasonable and necessary.

If a use is identified as not indicated by the Centers for Medicare and Medicaid Services (CMS) or the FDA, or if a use is specifically identified as not indicated in one or more of the compendia listed, or if the contractor determines, based on peer-reviewed medical literature, that a particular use of a drug is not safe and effective, the off-label usage is not supported and, therefore, the drug is not covered.

50.4.5.1 - Process for Amending the List of Compendia for Determination of Medically-Accepted Indications for Off-Label Uses of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

(Rev. 120, Issued: 01-29-10, Effective: 01-01-10, Implementation: 03-01-10)

A. Background

In the Physician Fee Schedule final rule for calendar year (CY) 2008, the CMS established a process for revising the list of compendia, as authorized under section 1861(t)(2) of the Social Security Act, and also established a definition for "compendium." At 42 CFR 414.930(a), a compendium is defined "as a comprehensive listing of FDA-approved drugs and biologicals or a comprehensive listing of a specific subset of drugs and biologicals in a specialty compendium, for example, a compendium of anti-cancer treatment." A compendium: (1) includes a summary of the pharmacologic characteristics of each drug or biological and may include information on dosage, as well as recommended or endorsed uses in specific diseases; (2) is indexed by drug or biological, and, (3) effective January 1, 2010, pursuant to section 182(b) of the Medicare Improvements for Patients and Providers Act (MIPPA), has a publicly transparent process for evaluating therapies and for identifying potential conflicts of interests. See 42 CFR 414.930(a); 72 FR 66222, 66404, and 74 FR 61901.

B. Desirable Characteristics of Compendia

CMS increased the transparency of the process by incorporating a list of desirable compendium characteristics outlined by the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) as criteria for decision-making. The list of desirable compendium characteristics was developed by the MedCAC during a public session on March 30, 2006. T he goal of this session was to review the evidence and advise CMS on the desirable characteristics of compendia for use in the determination of medically accepted indications of drugs and biologicals in anti-cancer therapy. As a result of this meeting, the MedCAC generated the following list of desirable characteristics:

- Extensive breadth of listings,
- Quick processing from application for inclusion to listing,
- Detailed description of the evidence reviewed for every individual listing,

- Use of pre-specified published criteria for weighing evidence,
- Use of prescribed published process for making recommendations,
- Publicly transparent process for evaluating therapies,
- Explicit "Not Recommended" listing when validated evidence is appropriate,
- Explicit listing and recommendations regarding therapies, including sequential use or combination in relation to other therapies,
- Explicit "Equivocal" listing when validated evidence is equivocal, and,
- Process for public identification and notification of potential conflicts of interest of the compendias' parent and sibling organizations, reviewers, and committee members, with an established procedure to manage recognized conflicts.

Furthermore, the provisions discussed in section 182(b) of MIPPA bring more uniformity in compendia conflict of interest disclosure practices and allow the public the ability to monitor how these policies impact compendia off-label recommendations.

C. Process for Changing List of Compendia

CMS will provide an annual 30-day open request period starting January 15 for the public to submit requests for additions or deletions to the compendia list contained on the CMS Web site at http://www.cms.hhs.gov/CoverageGenInfo/02_compendia.asp.

Complete requests as defined in section 50.4.5.1.D will be posted to the Web site annually by March 15 for public notice and comment. The request will identify the requestor and the requested action CMS is being asked to make to the list. Public comments will be accepted for a 30-day period beginning on the day the request is posted on the Web site. In addition to the annual process, CMS may generate a request for changes to the list at any time an urgent action is needed to protect the interests of the Medicare program and its beneficiaries.

D. Content of Requests

For a request to be considered complete, and therefore accepted for review, it must include the following information:

- The full name and contact information (including the mailing address, e-mail address, and telephone number) of the requestor. If the requestor is not an individual person, the information shall identify the officer or other representative who is authorized to act for the requestor on all matters related to the request.

- Full identification of the compendium that is the subject of the request, including name, publisher, edition if applicable, date of publication, and any other information needed for the accurate and precise identification of the specific compendium.

- A complete, written copy of the compendium that is the subject of the request. If the complete compendium is available electronically, it may be submitted electronically in place of hard copy. If the compendium is available online, the requestor may provide CMS with electronic access by furnishing at no cost to the Federal Government sufficient accounts for the purposes and duration of the review of the application in place of hard copy.

- The specific action that the requestor wishes CMS to take, for example to add or delete a specific compendium.

- Detailed, specific documentation that the compendium that is the subject of the request does or does not comply with the conditions of this rule. Broad, nonspecific claims without supporting documentation cannot be efficiently reviewed; therefore, they will not be accepted.

- A publicly transparent process for evaluating therapies, which includes the following: (1) internal or external request for listing of a therapy recommendation, including criteria used to evaluate the request (the complete application), (2) listing of all the evidentiary materials reviewed or considered for inclusion in the compendium (3) listing of all individuals who substantively participated in the review and development of the request, and (4) minutes and voting records of meetings for the review and disposition of the request. The information from an internal or external request for inclusion of a therapy in a compendium are available to the public for a period of not less than 5 years, which includes availability on the compendium's Web site for a period of not less than 3 years, coincident with the compendium's publication.

- A publicly transparent process for identifying potential conflicts of interests that provides: (1) direct or indirect financial relationships, and (2) ownership or investment interests that exist between individuals or the spouse or minor child of individuals who have substantively participated in the development or disposition of compendia recommendations, and the manufacturer or seller of the drug or biological being reviewed by the compendium. This information shall be identified and made timely available in response to a public request for a period of not less than 5 years, which includes availability on the compendium's Web site for a period of not less than 3 years, coincident with the compendium's publication.

A request may have only a single compendium as its subject. This will provide greater clarity to the scope of the Agency's review of a given request. A requestor may submit multiple requests, each requesting a different action.

E. Submission of Requests

Requests must be in writing and submitted in one of the following two ways (no duplicates please):

1. Electronic requests are encouraged to facilitate administrative efficiency. Each solicitation will include the electronic address for submissions.

2. Hard copy requests can be sent to: Centers for Medicare & Medicaid Services, Coverage and Analysis Group, Mailstop C1–09–06, 7500 Security Boulevard, Baltimore, MD 21244.

Allow sufficient time for hard copies to be received prior to the close of the open request period.

F. Review of Requests

CMS will consider a compendium's attainment of the desirable characteristics specified in 50.4.5.1.B when reviewing requests. CMS may consider additional, reasonable factors in making a determination. For example, CMS may consider factors that are likely to impact the compendium's suitability for this use, such as a change in the compendium's ownership or affiliation, and the standards applicable to the evidence considered by the compendium. CMS may consider that broad accessibility by the general public to the information contained in the compendium may assist beneficiaries, their treating physicians, or both, in choosing among treatment options. CMS will also consider a compendium's grading of evidence used in making recommendations regarding off-label uses, and the process by which the compendium grades the evidence. CMS may, at its discretion, combine and consider multiple requests that refer to the same compendium, even if those requests are for different actions. This facilitates administrative efficiency in the review of requests.

G. Publishing Review Results

CMS will publish decisions on the CMS Web site within 90 days after the close of the public comment period.

(This instruction was last reviewed by CMS in December 2009.)

50.4.6 - Less Than Effective Drug

(Rev. 1, 10-01-03)
B3-2049.4.C.5

This is a drug that has been determined by the Food and Drug Administration (FDA) to lack substantial evidence of effectiveness for all labeled indications. Also, a drug that has been the subject of a Notice of an Opportunity for a Hearing (NOOH) published in the "Federal Register" before being withdrawn from the market, and for which the Secretary has not determined there is a compelling justification for its medical need, is considered less than effective. This includes any other drug product that is identical, similar, or related. Payment may not be made for a less than effective drug.

Because the FDA has not yet completed its identification of drug products that are still on the market, existing FDA efficacy decisions must be applied to all similar products once they are identified.

50.4.7 - Denial of Medicare Payment for Compounded Drugs Produced in Violation of Federal Food, Drug, and Cosmetic Act

(Rev. 1, 10-01-03)
B3-2049.4.C.6

The Food and Drug Administration (FDA) has found that, from time to time, firms established as retail pharmacies engage in mass production of compounded drugs, beyond the normal scope of pharmaceutical practice, in violation of the Federal Food, Drug, and Cosmetic Act (FFDCA). By compounding drugs on a large scale, a company may be operating as a drug manufacturer within the meaning of the FFDCA, without complying with requirements of that law. Such companies may be manufacturing drugs, which are subject to the new drug application (NDA) requirements of the FFDCA, but for which FDA has not approved an NDA or which are misbranded or adulterated. If the FDA has not approved the manufacturing and processing procedures used by these facilities, the FDA has no assurance that the drugs these companies are producing are safe and effective. The safety and effectiveness issues pertain to such factors as chemical stability, purity, strength, bioequivalency, and biovailability.

Section 1862(a)(1)(A) of the Act requires that drugs must be reasonable and necessary in order to by covered under Medicare. This means, in the case of drugs, the FDA must approve them for marketing. Section 50.4.1 instructs carriers and intermediaries to deny coverage for drugs that have not received final marketing approval by the FDA, unless instructed otherwise by CMS. The Medicare Benefit Policy Manual, Chapter 16, "General Exclusions from Coverage," §180, instructs carriers to deny coverage of services related to the use of noncovered drugs as well. Hence, if DME or a prosthetic device is used to administer a noncovered drug, coverage is denied for both the nonapproved drug and the DME or prosthetic device.

In those cases in which the FDA has determined that a company is producing compounded drugs in violation of the FFDCA, Medicare does not pay for the drugs because they do not meet the FDA approval requirements of the Medicare program. In addition, Medicare does not pay for the DME or prosthetic device used to administer such a drug if FDA determines that a required NDA has not been approved or that the drug is misbranded or adulterated.

The CMS will notify the carrier when the FDA has determined that compounded drugs are being produced in violation of the FFDCA. The carrier does not stop Medicare payment for such a drug unless it is notified that it is appropriate to do so through a subsequent instruction. In addition, if the carrier or Regional Offices (ROs) become aware that other companies are possibly operating in violation of the FFDCA, the carrier or RO notifies:

Centers for Medicare & Medicaid Services
Center for Medicare Management
7500 Security Blvd.
Baltimore, MD 21244-1850

50.4.8 - Process for Amending the List of Compendia for Determination of Medically-Accepted Indications for Off-Label Uses of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

50.5 - Self-Administered Drugs and Biologicals

(Rev. 1, 10-01-03)
B3-2049.5

Medicare Part B does not cover drugs that are usually self-administered by the patient unless the statute provides for such coverage. The statute explicitly provides coverage, for blood clotting factors, drugs used in immunosuppressive therapy, erythropoietin for dialysis patients, certain oral anti-cancer drugs and anti-emetics used in certain situations.

50.5.1 - Immunosuppressive Drugs

(Rev. 1, 10-01-03)
A3-3112.4.B.3, HO-230.4.B.3, AB-01-10

Until January 1, 1995, immunosuppressive drugs were covered under Part B for a period of one year following discharge from a hospital for a Medicare covered organ transplant. The CMS interpreted the 1-year period after the date of the transplant procedure to mean 365 days from the day on which an inpatient is discharged from the hospital. Beneficiaries are eligible to receive additional Part B coverage **within** 18 months after the discharge date for drugs furnished in 1995; **within** 24 months for drugs furnished in 1996; **within** 30 months for drugs furnished in 1997; and **within** 36 months for drugs furnished after 1997.

For immunosuppressive drugs furnished on or after December 21, 2000, this time limit for coverage is eliminated.

Covered drugs include those immunosuppressive drugs that have been specifically labeled as such and approved for marketing by the FDA. (This is an exception to the standing drug policy which permits coverage of FDA approved drugs for **nonlabeled** uses, where such uses are found to be reasonable and necessary in an individual case.)

Covered drugs also include those prescription drugs, such as prednisone, that are used in conjunction with immunosuppressive drugs as part of a therapeutic regimen reflected in FDA approved labeling for immunosuppressive drugs. Therefore, antibiotics, hypertensives, and other drugs that are not directly related to rejection are not covered.

The FDA has identified and approved for marketing the following specifically labeled immunosuppressive drugs. They are: