Fraud Issues in Off-Label Promotion

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Food, Drug and Cosmetics Act

- Manufacturer of "new drugs" must demonstrate to FDA that they are safe and effective for each intended use. 21 U.S.C. 331(d)
- 21 U.S.C.331(a) Prohibits distribution of misbranded drug, including where label includes information about unapproved uses

Labeling

- Reviewed by FDA
- Specifies risks and benefits
- Gives indications and claims of benefits
- Pre-clinical and clinical trial results
- Drug must be safe and effective for all proposed claims. 21 CFR 201.100(d)

Promotion

- Claims in promotional “labeling” or advertising must be consistent with approved labeling. 21 CFR 202.1(e)(4)
- False or misleading representations with respect to another drug renders label “misbranded” 21 CFR 201.6

FDCA Remedies

- Administrative seizure of drugs. 21 USC 334(a)
- Injunctions against unlawful promotional activities. 21 USC 332(a)
- Production Step-downs
- Criminal Penalties for off-label marketing. 21 USC 333(a)

Medicaid Reimbursement

- Medicaid reimbursement available only for "covered outpatient drugs." 42 U.S.C. 1395b(i)(10)
- Covered Outpatient drugs exclude those "used for a medical indication which is not a medically accepted indication." 1396r-8(k)(6) A medically accepted indication includes FDCA approved use or use included in specified drug compendia. 1396r-8(g)(1)(B)(i)

Medicaid Reimbursement (Cont.)

- Prescription for off-label use of drug not included in identified compendia is not Medicaid reimbursable.
  - U.S. ex rel. Franklin v. Parke-Davis, 147 F. Supp. 2d 30, 44 (D. Mass. 2001)

Prosecution

U.S. v. Genentech, Inc. (N.D.Ca. 1999). Guilty plea to Introduction of Misbranded Drug in Interstate Commerce. 21 U.S.C. 331(a), 352.

Fine $30 million

Restitution to Medicaid and CHAMPUS $20 million

USA v. Genentech, Inc.

Protropin approved and labeled "only for long-term treatment of children who have growth failure from lack of adequate endogenous growth hormone secretion."

Genentech promoted for short stature for which drug not approved under Section 355.

Genentech introduced Protropin into interstate commerce intending it to be used for medical conditions for which it had not been approved and not been shown to be safe and effective.

In so doing, Genentech acted with intent to defraud and mislead FDA.

Qui tam

U.S. ex rel. Franklin v. Parke-Davis, Division of Warner-Lambert, 147 F. Supp. 2d 30 (D.Mass. 2001)

Alleged False Claims Act violation in submission of off-label prescriptions of drug to Medicaid stated a claim for fraud under the FCA where

- Drug was not reimbursable
- Misrepresented safety and efficacy
- Paid kickbacks to physicians

Off-label Marketing is Actionable under FCA

U.S. ex rel. Franklin v. Parke-Davis, (D. Mass., August 22, 2003)(Saris, J.)

- Falsehoods to physicians about neurontin's safety or efficacy to induce prescription for uses ineligible for Medicaid reimbursement are probative of false claims. Truthful off-label marketing (ineligible for federal safe harbors) accompanied by financial incentives like kickbacks would also suffice as evidence of false claims.
- Where states do not reimburse for off-label prescriptions, a reimbursement request for an off-label, non-compendium prescription constitutes a false claim.

Evidence

Rates of off-label prescriptions before and after physician conferences hosted by mfr

Market research reports recording doctors' state of mind after marketing meetings

Role of Mfr in prescribing activity

Small market for approved use/Large sales force

Financial incentives for off-label use, only

Failure to identify company funding for research, articles, presentations

Health consequences from off-label use

First Amendment Issues

- Washington Legal Foundation v. Friedman, 13 F.Supp. 2d 51 (d.D.C. 1998)
- Washington Legal Foundation v. Henney, 56 F.Supp. 2d 16, 18-19 (D.D.C 1999)
- Washington Legal Foundation v. Henney, 202 F.3d 331, 335 (D.C. Cir. 2000)
- Illinois ex rel Madigan v. Telemarketing Associates, Inc. __ U.S. ___ (May 5, 2003)