Lessons from GlaxoSmithKline's $3 billion settlement in the US

Kai Peters analyses the biggest ever healthcare fraud settlement with the US government.

On 2 July, the US Department of Justice announced that GlaxoSmithKline had agreed to plead guilty and to pay a record $3 billion to resolve its criminal and civil liability related to off-label promotion and other activities between 1994 and 2007 related to multiple prescriptions drugs.

As reported elsewhere in this issue, GSK agreed to plead guilty to three criminal counts, including two counts of introducing misbranded drugs and one count of failing to report safety data about another drug. GSK also agreed to resolve civil liabilities with the federal government and states.

This analysis of the settlement focuses primarily on the aspects relating to the integral allegations of off-label promotion and considers how pharmaceutical companies might avoid similar prosecution.

The Food, Drug and Cosmetic Act prohibits the introduction, or delivery for introduction, into interstate commerce of any pharmaceutical that is adulterated or misbranded. When the Food and Drug Administration approves a drug for manufacture and sale within the US, the use or uses for which the drug is approved are stated in the labelling for the drug. Misbranding may be found when the label, advertising, or promotion for the drug contains information about unapproved uses. A drug company engages in off-label promotion when it promotes a drug for uses which are not approved uses as stated in the label. It is noteworthy that physicians are allowed to prescribe drugs for off-label uses and off-label use of drugs is widely recognised as a valuable medical practice. Furthermore, companies as a general matter are allowed to engage in scientific exchange on off-label uses when it receives unsolicited requests for information.

A key alleged GSK misbranding violation, as with many prosecutions of drug companies, was off-label promotion. With respect to improper promotion, GSK's case involved the following:

- The government alleged that from January 1999 to December 2003 GSK illegally promoted Wellbutrin, approved at the time only for major depressive disorder, for off-label uses as it promoted the drug for weight loss, treatment of sexual dysfunction, substance addictions, and attention deficit hyperactivity disorder. Impermissible activities included paying millions to physicians for speaking at and attending meetings geared toward promoting use of the drug for the aforementioned uses, use of continuing medical education (CME) programmes to promote the drug for off-label uses, and use of sales representatives to promote the off-label uses.
- The government alleged that from April 1998 to August 2003, GSK engaged in impermissible off-label promotion of Paxil when it promoted Paxil for treating patients under the age of 18 when the FDA never approved the drug for use by minors. As detailed further below, the government also alleged that GSK sponsored activities to promote the use of Paxil in patients below 18 years.

In the wake of the GSK settlement, it is prudent for drug companies to analyse their own practices with respect to the following topics.

While it may seem to be a self-evident fact, companies should only provide balanced and non-misleading information. GSK's alleged off-label promotion included preparation, publishing, and distribution of a misleading journal article that misreported that a clinical trial of Paxil demonstrated efficacy in treating patients under the age of 18. To compound this misreporting, GSK allegedly did not make available data from other studies in which Paxil failed to demonstrate efficacy in such patients. Even when responding to unsolicited requests for information regarding off-label uses, companies should provide balanced information. Providing only favourable articles that purport to support the use of a drug for off-label uses should be avoided.

Clearly, a key impropriety in the GSK matter was the intersection of off-label promotion and the concurrent payment of physicians to participate in the off-label promotion. With respect to Wellbutrin, impermissible activities included paying millions to physicians for speaking at and attending meetings geared toward promotion of use of the drug for the aforementioned uses. With respect to Paxil, GSK allegedly paid a speaker to talk to an audience of physicians and paid for meals or spa treatments for attending physicians. In the wake of the GSK settlement, companies should closely track and analyse how and under what circumstances perks are being offered to and payments are made to physicians as they can turn physicians into agents of a company. Companies should avoid providing such perks when they coincide with events at which off-label information is being discussed. While companies can sponsor CME seminars, they must be very careful of the content of such seminars.

While GSK is facing record fines for its promotion of off-label uses including for its sponsoring of activities at which off-label information was exchanged, the FDA is currently analysing input from companies and other interested parties regarding how to define scientific exchange, what type of data should be exchanged, forums for exchange, and allowable participants in the exchange. The FDA solicited this input at least partially in response to a letter from multiple pharmaceutical companies requesting clarification about scientific exchange and off-label promotion considering the sometimes hazy line between them. Companies should monitor anticipated FDA guidance documents about scientific exchange so that they can provide information regarding off-label uses in a permissible manner.

It is a hot issue whether restrictions on drug companies providing truthful, non-misleading information in a sales context is protected by the First Amendment. In fact, the Second Circuit is currently considering that exact question in the *United States v Caronia* case in the wake of the recent case *Sorrell v IMS Health Inc*. In *Sorrell*, the US Supreme Court held that a Vermont law that restricted use of prescriber information by manufacturers and marketers (and not others) warranted heightened judicial scrutiny because the law was based on the content of speech and the identity of the speaker and violated the First Amendment's protection of commercial speech. Regardless, under the current regime, sales representatives should not be involved with the discussion of off-label uses for a drug. While sales reps will undoubtedly be the ones in a company organisation to initially receive requests for information about unapproved uses, companies should direct such healthcare provider questions to qualified personnel within a company.

With respect to Paxil, in 2004, GSK added a black box warning stating that antidepressants can increase the risk of suicidal thinking and behaviour in patients under 18 in short-term studies. GSK plead guilty to misbranding in that Paxil's labelling was false and misleading. Companies that manufacture non-generic drugs should have procedures in place to update the labelling for approved drugs in a timely manner. While pharmaceutical companies cannot actively promote drugs for off-label uses, they must monitor such off-label uses, including through adverse event reporting, journal articles and approved clinical trials, and take immediate steps to update labelling to warn of known adverse effects.

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