

Did minor flaws in a new drug reveal major flaws in company publication practices?

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Abstract

Pradaxa, a new drug for the treatment of blood clots, has been revealed to produce some negative side effects on a minor population of patients, according to a new study. However, the road leading to the publication of this study revealed that companies may be more concerned with protecting profits than publishing facts.

Keywords: Pradaxa, Blood clot, Warfarin

A multi-billion pharmaceutical shows a dark side, revealed by recent set of documents providing evidence of shady practices aimed at silencing an inconvenient research report in favour of maximising profits.

A recent article by the *New York Times* points to some disturbing practices followed by the makers of Pradaxa, also known as dabigatran, a drug currently prescribed against blood clots and stroke.^{1,2} Since its approval in 2010, Pradaxa has earned its maker more than \$2 billion in sales in the USA alone, being prescribed to more than 850 000 patients and gaining substantial terrain to warfarin, the most widespread generic drug for the treatment of these conditions.

In the article, the *New York Times* points to actions painting Boehringer Ingelheim (BI) as a pharma giant with a more keen interest in protecting benefits than learning the truth about an approved drug.² The controversy follows recently released court documents³ that are part of several ongoing lawsuits made by the family of deceased patients, who claim BI failed to properly inform them about the risk of taking Pradaxa.

Since its release, the drug has been linked with multiple cases of fatal bleeding, with more than 1000 deaths reported so far. The drug has also been linked to several adverse effects, including gastrointestinal problems, increase of heart attack risk, and most significantly, an increased risk of

haemorrhage.⁴ The European Medicines Agency identifies bleeding as the most serious side effect, occurring in 1 of 10 patients, as well as several incompatible conditions that may lead to adverse reactions in people who take the medicine.⁵

Despite the apparent risks, BI stands by the drug, pointing out that it is backed by the Food and Drug Administration, and by multiple clinical trials.¹ But, as the *New York Times* reports, the newly court-released documents, which include emails, memos, and internal presentations, reveal the concerns and efforts made by some company employees to deal with a new research report undermining Pradaxa's charms.²

The report, led by Paul A. Reilly, clinical programme director at BI, found that not all people, and in particular older patients, metabolise the drug in the same way and that a small population of patients would benefit from monitoring their blood.⁶ More specifically, the report finds that a small number of patients did not absorb the drug efficiently, whereas others absorbed it a bit too well, leading to an increased risk of bleeding.

The new research weakens one of Pradaxa's biggest selling points, namely, that unlike warfarin, blood tests are not a prerequisite for using it. This means that a wide variety of patients are able to access the drug, and the drug is favoured because it does not require nasty and constant blood tests to monitor its function, as warfarin does.

The original report went on to describe the ideal blood level of Pradaxa, saying that keeping patients within this range would be optimal for preventing stroke and bleeding.

Time for a change?

The controversy focuses on one important question: Can pharma companies be trusted with handling

their own results? The recently released evidence suggests several questionable internal practices, from both legal and ethical standpoints. In the end, the controversial paper was published, albeit not with all of its original results. According to a BI representative, the scientist decided not to report the suggested optimal dosage of this drug. Taken together, this story had a positive ending, as the results were seen outside of the company, but the difficult path up to publication suggests a worrying underlying problem.

According to the *New York Times*, before the publication of the research report, employees from different levels questioned the plans to publish the report. Their main concern was how the results may ‘negate a decade’s worth of work proving that patients taking Pradaxa would not need regular tests’.² Also, concern was raised that the results would not help in the company’s race against other new anticoagulants, like Xarelto and Eliquis.

Regarding all these issues and the court-released documents, BI claimed that the research results ‘represent small fragments of the robust discussion and debate that is a vital component in all scientific inquiry, and in the research and development of any important medication such as Pradaxa’. In practice, BI will now have to re-think its original strategy which sold Pradaxa as a one-size-fit-all drug that requires no testing, which is a positive outcome.

Now the ball is in the court of regulators, who ought to question the legal and ethical integrity of

big pharma companies and decide if they need a hand in deciding whether profits are more important than safety, even if the safety issues involve just a small number of patients.

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