Pharmaceuticals

Shock to the system

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Cholesterol drugs are under attack

"I SEE profound consequences arising from this," says Steven Nissen of the Cleveland Clinic, an American research hospital. Dr Nissen, a leading cardiologist, is up in arms over the way Merck and Schering-Plough, two American pharmaceutical giants, have handled a clinical trial of Vytorin, a blockbuster anti-cholesterol drug produced jointly by the two firms. Could this controversy upend the $25 billion cholesterol-fighting industry?

For years, the drugs of choice in combating heart disease have been statins such as Pfizer's Lipitor and AstraZeneca's Crestor. Concerned that the patent for its own statin, Zocor, was due to expire in 2006, Merck found a clever way to rejuvenate its franchise. It combined Zocor with Zetia, a cholesterol drug developed by Schering-Plough, to create Vytorin. (Statins reduce the formation of so-called "bad cholesterol", or LDL, in the liver; Zetia reduces its absorption.) But the Vytorin study, completed nearly two years ago and released only in January, found that on one important measure, the pricey branded drug was no more effective than the generic version of Zocor on its own, which costs one-third as much.

Merck and Schering-Plough insist they have done nothing wrong, and are adamant that Vytorin remains an important drug. On January 25th America's Food and Drug Administration (FDA) said it would scrutinise the study's results over the next eight months. A committee of the House of Representatives is also reviewing the handling of the study. Andrew Cuomo, New York's attorney-general, launched his own investigation on January 26th. His office will examine whether senior executives engaged in insider trading after learning of the results of the study, and whether Vytorin's lavish marketing campaign, which continued to run after the study was completed, violated the state's laws on false advertising claims. Meanwhile, several class-action suits have been filed in New Jersey, the home state of both pharmaceutical firms.

These legal and political troubles for Merck and Schering-Plough have been accompanied by a frenzy of negative media coverage and a public outcry over Vytorin, a popular drug which was prescribed 22m times in America last year, raising wider questions for the industry. Some are even challenging the scientific orthodoxy underpinning anti-cholesterol drugs,

which maintains that reducing the level of LDL cuts the risk of heart disease.

Viren Mehta, an industry expert, calculates that global sales of Vytorin and Zetia will fall by 10% in 2008 and remain flat until 2011, when a more detailed study of Vytorin will be completed. Sales of Lipitor and other statins unrelated to the Vytorin study have already been hit. But John Boris of Bear Sterns, an investment bank, reckons this is just a temporary setback caused by irresponsible media reports, and that sales will pick up again before long.

It is probably too soon to assess the damage to Vytorin. If doctors and patients grow skittish and stick with plain old statins instead, as they are now doing, that could deal a big blow to its prospects. Roger Blumenthal of Johns Hopkins University says Vytorin should not be tried as the first anti-cholesterol remedy for new patients: statins should. Only if patients reach the maximum tolerable dose of statins, or face unbearable side effects, should they try Vytorin. If that advice were really followed, however, it would wipe out much of the drug's future earnings, because some 40-45% of doctors, Mr Boris estimates, prescribe Vytorin right away as a “front line” therapy. Daniel Jones, head of the American Heart Association, blames the aggressive marketing tactics of drug companies for pushing doctors into prescribing Vytorin in the first instance.

Vytorin may yet have a bright future as a targeted remedy for a much smaller population group, rather than as a blockbuster. And even Dr Nissen, a leading critic of Vytorin, concedes that those claiming that all cholesterol science is bunk are going too far; he thinks statins, at least, have a bright future. The lasting effect of the Vytorin saga, he suggests, may be to change the way that drug trials are conducted. At the moment the FDA very rarely asks companies to conduct large-scale follow-up trials of new drugs after launch, and even when it does, its requests are often ignored. In future, regulators are more likely to insist on such trials—and on the timely disclosure of their results. As Merck and Schering-Plough are discovering, sunlight can be a powerful disinfectant.