

Obesity drugs: too much harm, for far too long

In 2016, a British team studied the causes for the market withdrawals of weight-loss drugs. They identified 25 drugs that had been withdrawn from markets around the world between 1964 and 2009. The mechanism of 22 of these drugs involved monoamine neurotransmitters (dopamine, noradrenaline or serotonin); examples include *benfluorex*, *fenfluramine*, *phentermine* (combined with *topiramate* in the United States) and *sibutramine*. One drug, *rimonabant*, was a cannabinoid derivative, and the two others acted on the thyroid (1).

80% of the market withdrawals were based on data from spontaneous reports, involving cardiac disorders for 8 drugs, psychiatric disorders for 7 drugs, and abuse or dependence for 13 drugs. Drug-attributed deaths had occurred with 7 of the drugs. The median time between market introduction and the first report of a serious adverse effect was 10 years; and the median time between the first report of a serious adverse effect and the first market withdrawal anywhere in the world was 11 years.

Fenfluramine was marketed for 24 years before its worldwide withdrawal in 1997 for heart valve disease. *Benfluorex* was marketed in France for 33 years before its withdrawal in 2009 for cardiotoxicity; yet the heart valve disorders resembled those caused by *fenfluramine* and the chemical structures of these two drugs are very similar (2). In France, *phentermine* was marketed from 1962 to 1988. *Sibutramine* was withdrawn in Europe in 2010, about 9 years after authorisation; and *rimonabant* was withdrawn in Europe in 2009, about 2 years after authorisation (1,3,4). Herbal weight-loss products were excluded from this study. In the late 1990s, dozens of patients in Europe developed chronic kidney disease due to weight-loss products supposedly containing the plant *Stephania tetrandra*. These herbal products contained another plant, belonging to the *Aristolochia* genus. About half of the patients developed a urinary tract cancer (5).

It is shocking how many times weight-loss drugs have been marketed after similar drugs had been withdrawn due to serious adverse effects. Many patients were exposed to their harms for many years. Health authorities should take note that those who cannot remember the past are condemned to repeat it, and demand greater assurances regarding the efficacy and safety of these drugs before allowing them onto the market.

Prescrire

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2- Prescrire Editorial Staff "Benfluorex: increasing reports of valve disorders" *Prescrire Int* 2010; **19** (105): 17.

3- Prescrire Editorial Staff "Topiramate + phentermine. An excessively dangerous appetite-suppressant combination" *Prescrire Int* 2013; **22** (136): 61-64.

4- Prescrire Editorial Staff "Rimonabant: marketing authorisation suspended... at last!" *Prescrire Int* 2009; **18** (100): 61.

5- Prescrire Rédaction "Insuffisance rénale et cancer des voies urinaires dus à des plantes chinoises" *Rev Prescrire* 2001; **21** (214): 124.