



Many modern ethicists would chortle at the idea that a physician should always treat, but there is no safe option. If the physician is determined to do his or her best with the resources at hand, treating those who are most likely to benefit when there are limited resources, then the population and the patient will trust him or her. It is up to some other agency to restrain him or her if that is necessary.

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**[One of the authors responds:]**

As a practising internist, I care for dying patients every day. My patients and their families do not always want all the treatment I could provide, and I respect their choices. I doubt many of them would accept Dr. Ney's suggestion that a physician should always treat, based on the "immutable guidelines" of "ancient medicine."

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**Weighing benefits and risks  
of drug to treat obesity**

A press release by Servier Canada was sent to health care professionals to clarify the details of an international study of appetite-suppressant drugs and the risk of primary pulmonary hypertension (PPH).<sup>1</sup> The study in question is a case-control study by Abenhaim and associates<sup>2</sup> that appeared in the *New England Journal of Medicine*. In the interest of greater clarity and balance,

I would like to offer a few details that may have been inadvertently omitted by Servier Canada.

As noted in the press release, the study by Abenhaim and associates is an epidemiologic one. Such studies do not prove cause and effect but only show associations. Most of what we now know, and what we will learn in the future, about the adverse effects of drugs, come from epidemiologic studies. In the study by Abenhaim and associates, dexfenfluramine and fenfluramine were the most commonly used appetite suppressants. Servier Canada received approval to market dexfenfluramine from the Health Protection Branch of Health Canada in July 1996.

The press release mentions the editorial by Manson and Faich<sup>3</sup> that accompanied the study by Abenhaim and associates, but does not discuss the controversy surrounding the editorial. Manson and Faich concluded that "the possible risk of pulmonary hypertension associated with dexfenfluramine is small and appears to be outweighed by benefits when the drug is used appropriately" and that the drugs could prevent an estimated 280 deaths per million obese people treated per year. Absent from this editorial and from the press release by Servier Canada are 2 sentences from the manufacturer's package insert that accompanies dexfenfluramine in the US: "The long-term effects of Redux on the mortality and morbidity associated with obesity have not been established," and "The safety and effectiveness of Redux beyond 1 year has not been established."<sup>4</sup> A recent editorial in the *New England Journal of Medicine* by its editors, Angell and Kassirer,<sup>5</sup> confirms that Manson and Faich have a financial connection with the companies that manufacture and market Redux. The editorial states, "We did not become aware of the essential features of these associations until 3 days before the publication date, when the first of many re-

porters phoned us about the conflict of interest." The editors were not satisfied with Manson and Faich's explanation for their failure to disclose fully their financial arrangements.

Current dexfenfluramine labelling in the US includes a boldface warning about the risk of PPH (odds ratio 9.1, 95% confidence interval 2.6 to 31.5).<sup>4</sup> On the basis of the results of the study by Abenhaim and associates, the labelling in the US requires a revision to reflect a higher estimate of the risk of PPH with use of the drug for more than 3 months (odds ratio 23.1, 95% confidence interval 6.9 to 77.7).<sup>6</sup>

In its press release, Servier Canada points out that it developed a fenfluramine product (Ponderal and Ponderal Pacaps) for the short-term treatment of obesity (less than 3 months), and that this drug has been available in France since 1964 and in Canada since 1972. It also notes that it developed a product (Redux) for long-term use and that this drug has been available in France and Europe since 1987. However, it does not mention the European view of the safety and effectiveness of this drug. In the United Kingdom in 1992, the Committee on Safety of Medicines advised physicians not to prescribe dexfenfluramine for longer than 3 months because of the risk of PPH.<sup>7</sup> The UK authorities specifically stated that "the serious nature of this reaction is nevertheless cause for concern, especially in relation to the lack of evidence on long-term benefit associated with these drugs." The French authorities have made similar recommendations that appetite suppressants, including dexfenfluramine, should be considered second-line treatment after failure of appropriate dietary measures and that their use should be limited to 3 months.<sup>8</sup>

If dexfenfluramine is offered to the Canadian public as a solution to a serious public health problem, the risk of PPH, with a 4-year mortality rate of 45%, must be evaluated in relation