



► said they remembered discussing their life expectancy with their physician. Patients with cancer were more likely than other patients to discuss their life expectancy with their doctor (26% versus 13%).

Among the 338 patients who did not remember having discussed their prognosis with their doctor, 143 patients (44%) said they would be interested in having such a conversation, while the other 185 patients (56%) said they would not (b)(1).

30% of the interviewed family members said they had discussed the patient's prognosis with the doctor, and nearly 90% of those who had not yet had this discussion said they would like to do so (1).

**Mostly satisfied.** Patients who discussed their life expectancy with their doctors were more satisfied than other patients with the doctor-patient relationship and with the treatment decision-making process (77.9% versus 72.4%) (1).

Patients who were in agreement with family members about their life expectancy were more likely to be satisfied with communication and decision-making than those who were not (77.3% versus 69.3%) (1).

**Communicate tactfully.** According to this survey, not all terminally ill patients want to discuss their life expectancy, while not all of those who would like to do so have been given the opportunity.

Healthcare professionals should take note of these findings: paying attention to their patients' wishes and discussing their life expectancy with those who want to do so, as well as with family members, can improve satisfaction with end of life care (2).

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#### Selected references from Prescrire's literature search.

1- Heyland D et al. "Discussing prognosis with patients and their families near the end-of-life: impact on satisfaction with end-of-life care" *Open Medicine* 2009; **3** (2): 101-110.

2- Fierens M "Pour des patients coresponsables des décisions de soins" *Rev Prescrire* 2010; **30** (322): 620-622.



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## Mediator<sup>o</sup> 150 mg - Sous-titre censuré

This book relates the story of a dangerous drug and one doctor's fight for patients' health (1).

**Clinical observation and attention to pharmacovigilance.** The author of this book is a pulmonologist who, while she was a house officer in 1990, was already aware of cases of pulmonary arterial hypertension in young adults, an uncommon disorder caused by *dexfenfluramine*, which led to its market withdrawal in 1999.

Years later, at Brest University Hospital where she works, she was struck by the coincidence between the use of *benfluorex* (marketed in France since 1976 under the brand name Mediator<sup>o</sup>) and cases of pulmonary arterial hypertension, serious heart valve disease and heart valve replacement surgery. She remembered the warnings she had read about in *Prescrire*, which regularly reminds its readers that *benfluorex* is a *fenfluramine* derivative, and that it is an amphetamine appetite suppressant. A discussion with *Prescrire* provided her with more information about the exact chemical nature of the drug, as information on the subject was rare or nonexistent elsewhere.

**Analysis of adverse effects and case-control studies.** This doctor is tenacious, and above all, she did not want to see any more female patients, some of whom were young, having to undergo heart valve surgery, and dying after taking *benfluorex*, which she gradually realised to be the case. *Benfluorex* was marketed for more than thirty years in France as « *an adjuvant treatment for diabetes* », but had no proven efficacy in this indication. It was widely prescribed, in an unapproved use to help patients lose weight as well.

After gathering and analysing all cases of heart valve disease at Brest University Hospital, she conducted a case-control study, and alerted the French drug regulatory agency (Afsaps) (2). Neither the company marketing Mediator<sup>o</sup> nor Afsaps, which is supposed to protect patients and their health, displayed a sense of urgency concerning the serious adverse effects observed in patients taking *benfluorex*. The hearings held by the Pharmacovigilance Committee or other Afsaps technical committees, which are described in the book, do not reflect well on the agency: no information was provided about the participants, and there

was certainly no mention of any conflicts of interest. No information was provided about who attended the hearings and whether or not participants worked for the pharmaceutical company. And healthcare professionals who attend these hearings to present their worrisome discoveries are not exactly well treated. The author writes that "(...) rather than discussing issues with Afsaps, one 'negotiates'" (our translation).

**A great service to patients.** David versus Goliath perhaps, an imbalance of power undoubtedly (a), but in the end, a healthcare professional who was anxious to understand and to protect patients won, by playing a role in the withdrawal of a drug that was clearly too dangerous (3).

This book illustrates how rare adverse effects can be detected through observation and clinical curiosity: it should encourage all healthcare professionals to become involved in pharmacovigilance, at the level of the patients they treat (b).

This book provides insights into the world of pharmaceuticals, with all of its inadequacies and their consequences, in a clear and straightforward manner. It is recommended reading for everyone, including patients, who are greatly indebted to such healthcare professionals.

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a- The website of *editions-dialogues.fr* states that "the pharmaceutical company Servier instituted proceedings against the book's publishers, *Éditions dialogues*, and requested that the phrase: "How many deaths?" be removed from the cover [Editor's note: the original subtitle of the book], on the grounds that it might cause serious damage to the company. It also states that the judge granted this request, writing that "the defendant (*Éditions dialogues*) does indeed minimise the impact of the title of its book by mentioning the fact that distribution of the product has now been suspended and that the damage would therefore not be great. However, this argument can be turned around. If, eventually, after analysis, the suspension is lifted, and distribution of products containing *benfluorex* resumes, the contentious statement could then damage the reputation of both the manufacturer and its product" (ref 5).

b- Clinical trials are not well suited to the study of adverse effects, and alone, they do not suffice to detect rare, potentially serious adverse effects (ref 6).

#### Selected references from Prescrire's literature search.

1- Frachon I "Mediator 150 mg : sous-titre censuré" *éditions-dialogues.fr*, Brest 2010: 148 pages, 15,90 €.

2- Prescrire Editorial Staff "Benfluorex: increasing reports of valve disorders" *Prescrire Int* 2009; **18** (105): 17.

3- Prescrire Editorial Staff "Benfluorex. EU marketing authorisation finally withdrawn" *Prescrire Int* 2010; **19** (109): 206.

4- Laporte JR "Pour une pharmacovigilance plus ambitieuse" *Rev Prescrire* 2010; **30** (319): 391-393.

5- Kermarec C "Irène Frachon: Mediator 150 mg". *éditions-dialogues.fr* accessed 8 July 2010.

6- Prescrire Editorial Staff "Evaluation of treatment risks: taking clinical data, pharmacology and patients characteristics into account" *Prescrire Int* 2010; **19** (105): 44-45.