New drugs: improve information about uncertainties

When new drugs enter the market, there is (sometimes great) uncertainty about their efficacy and adverse effects (1).

A Dutch team, including academics and employees of the Dutch Medicines Evaluation Board and the European Medicines Agency (EMA), studied the uncertainties described in the European public assessment reports of 121 drugs newly authorised in the European Union between 2011 and 2022 for an oncology indication. 800 uncertainties were identified, mostly relating to adverse effects (51%) and efficacy (40%). The median number of uncertainties per drug increased from 4 to 7 between 2011-2014 and 2019-2022, and from 1 to 3 for those concerning efficacy. Significantly more uncertainties were found for drugs with conditional marketing authorisation or marketing authorisation under exceptional circumstances, and for gene therapy products (2).

The situation is similar in the US, where more than 200 drugs have been granted accelerated approval since 1992, half of which were ultimately not shown to be effective (3).

Is this increasing uncertainty an acceptable price to pay for more rapid access to "innovative" drugs, as the US Food and Drug Administration (FDA) and others seem to suggest? Can a drug that has not been shown to represent a therapeutic advance be considered innovative? Wouldn't it be better to wait longer and have robust evidence? A British team put these questions to 870 adults affected by cancer as a patient (21%), or as a relative (81%) or friend (36%) of a patient. In a situation where a new drug has not been shown to extend survival, the respondents preferred to wait, on average, 8 months for weak evidence of longer survival, 16 months for more robust evidence, and 22 months for strong evidence (3).

In summary, the race to provide ever-earlier access to new drugs in Europe and the US could be based on regulators' incomprehension of what patients really want.

What information is available to patients about the uncertainties surrounding the evaluation of new drugs? None at all, if they only read the patient information leaflet concerned, since these documents make no mention of the uncertainties discussed in regulators' assessment reports, for example. This absence of information hinders their ability to make informed treatment decisions (1).

In Prescrire's contribution to the EMA's public consultation on improving patient information leaflets, we requested, among other things, that they include "*the uncertainties that remain, in particular when data (concerning a long-term benefit or adverse effect, for example) are lacking, or the level of evidence is too low*" (4).

Because, as acknowledged by the EMA's then Head of Research and Innovation in his contribution to a conference organised by Prescrire in 2021, "*sometimes the unknowns are even more important than what is known because, if you are not well-informed about the unknowns, you don't know if that unknown has ever been looked at*" (5).

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References **1-** Davis C et al. "Patients deserve better information on new drugs" *BMJ* 2024; 387; e08172010, 7 pages. **2-** Taams AC et al. "Uncertainties about the benefit-risk balance of oncology medicines assessed by the European Medicines Agency" *Esmo Open* 2024; 9 (12): 103991,13 pages. **3-** Forrest R et al. "Preferences for speed of access versus certainty of the survival benefit of new cancer drugs: a discrete choice experiment" *Lancet Oncol* 2024; 25 (12): 1635-1643. **4-** "EMA: two surveys about the patient leaflet" *Prescrire Int* 2024; 33 (265): 307. **5-** "Jordi Llinares: Sometimes the unknowns are even more important than what is known" *Prescrire Int* 2021; 30 (228): 194-195.