Look to the past

When a product arrives on the market, it doesn't appear out of nowhere. It has a past. It may be a slightly improved version of a well-established product, or one of several prototypes that have been in development for many years. Or perhaps a substance derived from a product that was abandoned because it proved to be of no value or too dangerous, etc. The story around the development of a new product always contains useful information on which to reflect, in order to understand and make informed decisions.

One example in the field of health care is the now-withdrawn drug *benfluorex* (formerly marketed as Mediator°), whose serious adverse effects could have been anticipated in light of past experience with the other amphetamine-like appetite suppressants (see, for example, "Mediator° disaster: the damning appeal judgement", *Prescrire Int* n° 265).

Or the gliflozins, which lower blood glucose by inhibiting sodium-glucose cotransporter 2 (SGLT2), and were shown in the mid-2010s to cause diabetic ketoacidosis. Again, this adverse effect could have been foreseen much earlier, since, back in the late 19th century, ketoacidosis had been reported with phlorizin, a naturally-occurring substance whose effects include SGLT2 inhibition (see "Memory can save lives", *Prescrire Int* n° 220).

Or the various cholesterol-lowering drugs developed since the 1960s. One of the lessons from their past is that an effect on a surrogate endpoint is no guarantee of an improvement in clinical outcomes (see "50 years of cholesterol-regulating drugs: what benefits?", *Prescrire Int* n° 174).

More recently, past experience with amyloid-beta-targeting drugs proved a source of valuable information, when, in 2025, *lecanemab* (Leqembi°) became the first of this class to be authorised in the European Union for Alzheimer's disease (see pp. 89-94 of this issue). The story of this class starts in the 1990s and involves the development of dozens of substances that lacked clinical efficacy, yet were shown to have serious adverse effects, including brain lesions. Before authorising *lecanemab*, drug regulatory agencies should have taken this information into account and demanded robust evidence, from at least two clinical trials, of sufficient clinical efficacy to make the risk of such serious adverse effects acceptable.

Various sources of information are used to assess whether a drug improves patient care, including clinical trial results and pharmacovigilance data. But it is also useful to look to the past and retrace its history.

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EDITORIAL