Prescrire International Editorial

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Early signals

Science takes time, but business is in a hurry. Most drug approval decisions are based on short-term clinical trials. In the absence of long-term clinical evidence, drug regulatory agencies gamble on early indicators.

When *aliskiren* was first licensed, the gamble was that there was a reasonable chance that its effect on a surrogate endpoint, blood pressure-lowering, would translate into a reduced incidence of cardiovascular events. In other words, a great deal of attention was paid to an early indicator of expected efficacy. The same level of attention was not paid to early indications of the risk of adverse effects.

Aliskiren is a renin inhibitor. The risk of cardiovascular and renal adverse effects provoked by the concomitant use of an angiotensin II receptor blocker (ARB) or ACE inhibitor did not elicit enough concern to contraindicate such combinations, as a precautionary measure.

A*liskiren* was reassessed 4 years after its market introduction: its efficacy remains unproven, but there is evidence that patients with diabetes taking *aliskiren* with ARBs or ACE inhibitors developed cardiovascular disorders and sometimes fatal renal failure (see page 176 of this issue).

If early indications of adverse effects had been afforded the same attention as early indicators of efficacy, more caution would have been exercised and *aliskiren* would not have been approved so hastily.

It is patients who pay, sometimes with their lives, for any ill-considered gamble on the harm-benefit balance.

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