

Flexibility

"With a large glass of water", "at least 30 minutes before eating or drinking", "during meals", "15 minutes before bedtime", etc.

From a practical point of view, medicines are tangible objects that come in various pharmaceutical forms (such as tablets, capsules or a solution for injection), each with its own packaging (including a box, container and patient leaflet). Healthcare professionals often specify how and when medicines should be taken when prescribing, dispensing or administering them, whether or not this information is included in the patient leaflet. These instructions are usually based on information provided in the summary of product characteristics (SmPC), but is the level of evidence sufficiently strong to serve as a basis for hard and fast rules?

Often, the data supporting these instructions come from pharmacokinetic studies performed in healthy volunteers. Less often, these data were obtained in clinical studies carried out in patients. And, even less often, from randomised trials with patient-relevant endpoints (see "Taking blood pressure-lowering drugs in the evening: major uncertainty regarding the benefit" p. 277 of this issue).

For some drugs, the link between a major adverse effect and the conditions of administration has been clearly demonstrated, for example: oesophageal ulceration caused by bisphosphonates, overdose of a drug with a narrow therapeutic index, or reduction in efficacy of certain drugs, such as *doxycycline*, when taken with dairy products or with antacids containing aluminium or magnesium.

For many other drugs, too little is known about how the conditions of administration influence the drug's efficacy or increase the risk of adverse effects, making it impossible to establish rules applicable to all patients. When the clinical evaluation data are insufficiently robust to serve as a basis for determining precisely when and how to take a drug, allowing each patient the leeway to do what feels and works best for them is a pragmatic option. Especially when the solution chosen by the patient helps alleviate certain adverse effects. An example? That of *levodopa*-containing medicines (see "When should levodopa be taken: with meals or between meals?" p. 279 of this issue).

A relatively flexible approach can therefore be adopted in many cases: *"no precise instructions need to be followed concerning when to take this drug: take it at the time of day that best suits you"*.

Prescribe