Combination drug therapy of hypertension has become more widely used in order to achieve the lower blood pressure goals currently recommended, especially for patients with diabetes mellitus and chronic kidney disease. When fixed-dose combination products are used, there may be an additional disincentive to perform drug dose titration when indicated due to what has been termed clinical inertia or therapeutic inertia. This is due, in part, to the need to write a new prescription for a higher dose combination product and the possible lack of flexibility of dose forms. In addition, one cannot easily titrate one component without changing the other(s). If a patient has an adverse effect, it is not possible to stop the allegedly responsible component (at least temporarily) while continuing the other without writing a new prescription, many of which are never filled.

Physicians tend not to bring patients to target blood pressure if it requires additional action. Most titration to goal blood pressure should be accomplished after initiation of a new medication, but later titration (either upward or downward) often becomes necessary as conditions change. The temptation, especially if the patient is fairly close to goal, is to ignore the need for additional medication. Alternatively, one must take the action of writing a new prescription or writing multiple prescriptions. All of this takes time and effort.

Successful titration can be achieved without writing a new prescription or writing multiple prescriptions. The tablets are color coded to allow for common colorblind patterns and marked so that instructions can be given by telephone just as one does with modifying the dose of other medications. The tablet structure shown in Figure 1 was could provide the essential benefits of traditional fixed-dose combination therapy—enhanced compliance and one co-pay—with the traditional advantage of two separate dosage forms, namely dosage flexibility. This use of ACCU-BREAK™ technology allows the tablet to be manufactured so that each of two drugs is formulated in layers at opposite ends of the tablet with an inactive layer placed in between. Drug “A” is separated from drug “B” by the inactive layer (“A-I-B”). The inactive area will generally be scored. The tablet is shaped and sized both for easy breaking and easy swallowing as a whole tablet. As long as a break in the inactive layer does not impinge upon either the “A” or “B” layer, the tablet can break irregularly by mass yet each half tablet (or “tablettes”) will contain the full dose of each drug. Each layer has its unique color and code marking.

REFERENCES


Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. BMJ. 2003;326:1419-1424.


LIMITATIONS

No product made with ACCU-BREAK technology is currently marketed. Multiple patents are pending and the processes dictated by regulatory agencies have been initiated. Patient education brochures and package inserts must be created in order to maximize the many potential benefits of these tablets and to minimize the risks of misunderstanding and misinformation as much as possible.