

Which medications can be split without compromising efficacy and safety?

EVIDENCE-BASED ANSWER

Split tablets of lisinopril are as effective as whole tablets of the same dose for hypertension (SOR: **B**, based on small randomized crossover study). Similarly, split tablets of atorvastatin, lovastatin, and simvastatin are no less effective for lowering cholesterol (SOR: **B**, based on retrospective

cohort studies). Extended-release, enteric-coated, or tablets that cannot be split accurately are not appropriate for splitting (SOR: **C**, based on observational studies); the accuracy of splitting also depends on device used and user skill (SOR: **C**, based on observational study) (**TABLE**).

CLINICAL COMMENTARY

Splitting scored tablets is efficacious and safe, but cost savings are often limited

The theoretical benefit of tablet-splitting is reduced prescription cost. Splitting scored tablets is already FDA-approved as safe and efficacious. However, the cost savings garnered by splitting these types of tablets is often limited. The biggest savings comes from splitting flat-priced tablets (costs of different dosage strengths are equal/similar), but these tablets are not usually scored. Splitting unscored tablets is considered “off-label” because each split tablet dose may not have equal drug

strength. However, splitting drugs with a long half-life and wide therapeutic index—such as those used to treat chronic asymptomatic conditions like hypertension or dyslipidemia—should pose minimal risk.

Be aware that recommending tablet-splitting to insured patients solely to spare them a copay—instructing a patient to take a half tablet to make a 30-day paid prescription cover 60 days—may be considered insurance fraud. However, this is not an issue for patients without prescription coverage.

Joseph Saseen, PharmD, FCCP, BCPS
University of Colorado Health Sciences Center, Denver

Evidence summary

Few studies have looked at the clinical effects of pill-splitting. A randomized trial (n=29) evaluated tablet-splitting by patients taking lisinopril for hypertension.¹ Patients were randomized to split tablets or whole tablets for 2 weeks, then crossed over to the other group for 2 weeks. There was no difference in blood pressures between groups.

A retrospective study of simvastatin evaluated 1098 patients taking whole tablets and 1098 patients converted to split tablets of the same dose.² There was no difference in average final low-density lipoprotein (LDL) cholesterol (111 ± 30 mg/dL vs 112 ± 32 mg/dL) or mean alanine aminotransferase (ALT) level.

Another retrospective study evaluated

John Noviasky, PharmD
St Elizabeth Medical Center,
Utica, NY

Vincent Lo, MD
SUNY Upstate Medical
University, Syracuse, NY; San
Joaquin General Hospital
Family Medicine Residency
Program, French Camp, Calif

Diane D. Luft, MSI
SUNY Upstate
Medical University,
Syracuse, NY

TABLE

Questions to consider before tablet-splitting

If you answer "NO" to any of these questions, reconsider the appropriateness of recommending tablet-splitting to a patient

Medication characteristics

- Is the tablet scored*?
- Is the tablet modified or extended release?
- Is the tablet a combination product?
- Is the tablet a critical dose product?
- Does the tablet crumble when split?
- Is the tablet film-coated or otherwise modified to mask taste or for some other reason?

*Some tablets without scoring may be split easily with tablet-splitting device.

Patient characteristics

- Is the patient physically capable of splitting the tablet (consider dexterity, strength, and visual acuity)?
- Will the patient's medication regimen remain manageable with tablet-splitting (in other words, will tablet-splitting make patient's regimen excessively complicated)?

FAST TRACK

The cost savings of splitting scored tablets is limited; but splitting unscored tablets is "off-label" because the splits may be unequal

tablet-splitting by 512 patients taking statins (atorvastatin, lovastatin, simvastatin).³ Cholesterol values after 12 or more weeks on a stable whole-tablet dose were compared with those 6 to 52 weeks after initiating tablet-splitting; no significant change was seen in total cholesterol or triglycerides. There was a statistically significant decrease in LDL (102 ± 28 vs 97 ± 29 mg/dL, $P < .001$), an increase in high-density lipoprotein (HDL) cholesterol (46 ± 12 vs 48 ± 12 mg/dL, $P < .001$), and an increase in aspartate aminotransferase (AST) (26 ± 8 vs 28 ± 10 units/L, $P < .001$), which was attributed to higher medication dosage from accidental ingestion of whole tablets and to diet and lifestyle modifications. Another retrospective evaluation of 109 patients with split atorvastatin or simvastatin found no significant difference in total cholesterol or LDL values after initiating the tablet-splitting program.⁴

Thirty patients aged 50 years or older, half of whom received instruction and a demonstration, evaluated 2 tablet-splitters with different blade positions and types of guide.⁵ One device (Apex Pill Splitter) produced more accurate results by 10% to 20% (P value not provided) with meto-

prolol, warfarin, and lisinopril tablets. Instructed patients were 1% to 10% more accurate, as were those with experience splitting warfarin tablets ($P = .003$).

In another study, 94 healthy volunteers (mean age, 46.2 years) each split 10 hydrochlorothiazide 25 mg tablets by hand. Forty-one percent of the split products were more than 10% off ideal weight; 12% of tablets were more than 20% off.⁶ Manufacturing regulations require that medication doses vary by less than 10% of the nominal dose. Another study using 5 medications found that 0% to 44% of split tablets deviated from ideal weight by 20%, depending on tablet shape.⁷

Surveys of patient acceptance of tablet-splitting report varied rates (3%–74%),^{3,6} In 1 study,¹ 89% and 97% said they would split tablets to save money for themselves or their health facility, respectively.

Experts recommend assessing patients for their physical (dexterity, strength, visual acuity) and cognitive ability to split tablets, as well as whether doing so saves money.⁸

Recommendations from others

The American Medical Society and American Pharmacists Association oppose mandatory tablet-splitting and recommend against splitting tablets that are modified-release, combination products, unscored, film-coated, friable, or dose-critical.

REFERENCES

1. Rindone JP. Evaluation of tablet-splitting in patients taking lisinopril for hypertension. *J Clin Outcomes Management* 2000; 7:22–24.
2. Parra D, Beckey NP, Raval HS, et al. Effect of splitting simvastatin tablets for control of low-density lipoprotein cholesterol. *Am J Cardiol* 2005; 95:1481–1483.
3. Gee M, Hasson NK, Hahn T, Ryono R. Effects of tablet-splitting program in patients taking HMG-Coa reductase inhibitors: analysis of clinical effects, patient satisfaction, compliance, and cost avoidance. *J Managed Care Pharm* 2002; 8:453–458.
4. Duncan MC, Castle SS, Streetman DS. Effect of tablet splitting on serum cholesterol concentrations. *Ann Pharmacother* 2002; 36:205–209.
5. Peek BT, Al-Achi A, Coombs SJ. Accuracy of tablet splitting by elderly patients. *JAMA* 2002; 399:451–452.
6. McDevitt JT, Gurst AH, Chen Y. Accuracy of tablet splitting. *Pharmacotherapy* 1998; 18:193–197.
7. Gupta P, Gupta K. Broken tablets: does the sum of the parts equal the whole? *Am J Health Syst Pharm* 1988; 45:1498.
8. Tablet splitting: evaluating appropriateness for patients. *J Am Pharm Assoc* 2004; 44:324–325.