



# The DUR Discovery

Exploring ways to improve pharmacotherapy

## Inappropriate Medications for the Elderly

by Chris Owens, PharmD

Inappropriate medication use in the elderly is associated with a substantial number of adverse drug reactions, worsening physical function, and excessive healthcare utilization. In the year 2000, medication-related problems were believed responsible for over 106,000 deaths and cost the US healthcare system in excess of \$85 billion. For these reasons, vigilant monitoring in the elderly population is

and reviewed by a number of experts in geriatric medicine and pharmacology under the direction of Dr. Mark Beers, these criteria have been utilized to identify individual and classes of medications to avoid in elderly patients. Beers list drugs are categorized as such because they are either lacking in efficacy and/or pose an unnecessarily high risk to elderly patients given that safer alternatives are available.

Table Ia: Beers List Drugs and Concerns\*

Drug	Concern
Benzodiazepines Diazepam Flurazepam	Prolonged sedation and increased risk of falls/fractures
GI antispasmodics Dicyclomine Hyoscyamine	Highly anticholinergic; uncertain effectiveness
Indomethacin	Produces most CNS adverse effects of the NSAID class
Meperidine	May cause confusion; many disadvantages over other opioids
Muscle Relaxants Carisoprodol Cyclobenzaprine	Poorly tolerated; anticholinergic and other adverse effects
Oxybutynin	Anticholinergic adverse effects
Pentazocine	Produces more confusion and hallucinations than other opioids
Propoxyphene	Few analgesic advantages over APAP; adverse effects of opioids
TCAs Amitriptyline Doxepin	Anticholinergic adverse effects

\* Adapted from reference 2

essential for both improving patient safety and relieving unnecessary economic burden on healthcare resources.<sup>1,2</sup>

“The Beers Criteria” are perhaps the most well-known consensus criteria for medication use in the elderly. Developed

Table Ia lists commonly prescribed Beers list drugs. It is important to note that while many elderly patients can and do tolerate many of these drugs, their use is associated with an increased risk for adverse events and therapy should be periodically reevaluated.<sup>2,3,4</sup>

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# Tablet Splitting: Cost Savings vs. Patient Safety

by Catherine Heyneman, MS, PharmD and Seth Thomas, PharmD Candidate

## The Pros of Tablet Splitting

The cost of prescription medications has continued to escalate, becoming the fastest rising component of US medical expenditures. Many prescription medications cost the same per tablet, regardless of the strength. Therefore, many health care providers have become proponents of tablet splitting: supplying the patient with twice the necessary dosage in half the quantity to reduce costs by approximately half. A quick review of Table 1b will give the reader an idea of the magnitude of cost savings tablet splitting can achieve.

Managed care has embraced the concept of tablet splitting, and many HMOs and insurers now mandate pill splitting for qualified medications. In fact, several major health insurance companies are offering free tablet splitters or reduced copays to their customers who agree to participate in tablet splitting. Washington's Regence Blue Shield, which covers 45,000 customers in the Seattle area, has estimated that if every eligible patient split tablets the resultant savings would be approximately \$5 million annually.<sup>1</sup> Florida's Medicaid program has reported a \$4 million annual savings by requiring patients to split Paxil® and Zoloft®.<sup>2</sup> An evaluation of newer psychotropic medications concluded that \$1.45 billion in medication costs could be saved annually in the US from tablet splitting of this drug class alone.<sup>3</sup>

Two evidence-based trials have investigated the clinical effect of splitting statins on serum cholesterol levels.<sup>4,5</sup> One trial demonstrated no statistically significant change in total cholesterol or LDL cholesterol as a result of switching from whole to split simvastatin or atorvastatin,<sup>4</sup> and the other actually resulted in a statistically significant (albeit not clinically relevant) decrease in LDL and increase in HDL after splitting atorvastatin, lovastatin and simvastatin.<sup>5</sup> Therefore, at least in the context of antihyperlipidemics, tablet splitting does not reduce clinical efficacy.

## The Cons of Tablet Splitting

There are several patient safety issues to be bear in mind when considering tablet splitting. First, will splitting a tablet give the patient an accurate dosage, and how crucial is this to achieving positive health outcomes? Several trials have attempted to answer this question.<sup>6-8</sup> All utilized United States Pharmacopeia (USP) criteria for acceptable weight variation between tablets (weight within 15% of the mean and variability no greater than 6% as assessed by standard deviation). Overall, between 41% and 73% of medications failed to achieve USP

uniformity criteria, but most fell within 20% of the desired weight. These numbers do not improve when pharmacists do the splitting; the variability seems to be inherent to the splitting process.

Would this level of variability adversely affect health-related patient outcomes? Certainly, tablet splitting should be avoided for medications with steep dose-response curves or narrow therapeutic windows such as Synthroid® or Lanoxin®. However, for many antihypertensives and psychotropics, clinical efficacy depends upon relatively long-term changes in neurotransmitter expression and receptor sensitivity – small variations in dosage would not be critical to effectiveness.

### Figure 1: Optimal Medication Characteristics for Good Tablet Splitting Outcomes

- Large enough to split by hand or to handle easily in a tablet splitter
- Maintains therapeutic integrity when split (not a controlled release or extended release formulation)
- Not enteric coated or film coated (film coating often masks bitter taste)
- Scored for easy splitting
- Not a drug that requires a finely calibrated dosage, such as Synthroid® or Depakote®
- Drugs with similar costs for different dosages (this maximizes cost savings)
- Splits cleanly and does not crumble

Not all medications are appropriate for tablet splitting. There are several product characteristics essential for successful pill splitting (see Figure 1). The medication should not be a controlled release or enteric coated formulation because splitting may cause rapid release of the medication or dissolution too early in the intestinal tract. Additionally, some medications, such as Biaxin® are film coated to mask a bitter taste which could result in noncompliance if split. The ideal tablet for splitting is scored, cleaves cleanly without crumbling, and costs the same amount of money regardless of dosage. The medications presented in Table 1b are all good candidates

**Table Ib: Annual Cost Savings Associated with Tablet Splitting of Selected Drugs**

Category	Medication	Original Dosage Regimen	New Dosage Regimen	Annual Cost Savings (based on AWP)	Comments
Antianxiety	BuSpar®	5 mg qd	15 mg 1/3 tab qd	\$43.59	Scored in thirds
		10 mg qd	15 mg 2/3 tab qd	\$2.11	
	buspirone	5 mg qd	15 mg 1/3 tab qd	\$24.12	Generic scored in thirds
		10 mg qd	15 mg 2/3 tab qd	\$2.01	
	Klonopin®	0.5 mg bid	1 mg ½ tab bid	\$331.42	Unscored
clonazepam	0.5 mg bid	1 mg ½ tab bid	\$234.73	Generic scored	
Antidepressants	Celexa®	20 mg qd	40 mg ½ tab qd	\$475.07	Scored
	citalopram	20mg qd	40mg ½ tab qd	\$423.65	Scored
	Lexapro®	10 mg qd	20 mg ½ tab qd	\$453.17	Scored
	Luvox®	50 mg qd	100 mg ½ tab qd	\$585.11	Scored
	fluvoxamine	50 mg qd	100 mg ½ tab qd	\$456.72	Generic scored
	Paxil®	20 mg qd	40 mg ½ tab qd	\$468.77	Unscored
	paroxetine	20 mg qd	40 mg ½ tab qd	\$439.70	Generic unscored
	Serzone®	100 mg bid	200 mg ½ tab bid	\$605.23	Unscored
	Zoloft®	50 mg qd	100 mg ½ tab qd	\$538.38	Scored
	Effexor®	50 mg qd	100 mg ½ tab qd	\$334.78	Scored*
	Remeron®	15 mg qd	30 mg ½ tab qd	\$535.77	Scored
mirtazapine	15 mg qd	30 mg ½ tab qd	\$480.65	Scored	
Antihyperlipidemics	Lipitor®	10 mg qd	20 mg ½ tab qd	\$248.52	Unscored
		20 mg qd	40 mg ½ tab qd	\$656.88	
		40 mg qd	80 mg ½ tab qd	\$656.88	
	Mevacor®	10 mg qd	20 mg ½ tab qd	\$64.52	Unscored octagonal shape
		20 mg qd	40 mg ½ tab qd	\$96.18	
	lovastatin	10 mg qd	20 mg ½ tab qd	\$57.94	Generic unscored
		20 mg qd	40 mg ½ tab qd	\$86.50	
	Pravachol®	20 mg qd	40 mg ½ tab qd	\$435.99	Unscored
		40 mg qd	80 mg ½ tab qd	\$847.35	
	Zocor®	10 mg qd	20 mg ½ tab qd	\$122.83	Unscored shield shape
		20 mg qd	40 mg ½ tab qd	\$838.59	
40 mg qd		80 mg ½ tab qd	\$838.59		
Antihypertensives	Atacand®	8 mg qd	16 mg ½ tab qd	\$270.39	Unscored
		16 mg qd	32 mg ½ tab qd	\$95.47	
	Avapro®	150 mg qd	300 mg ½ tab qd	\$239.32	Unscored
	Cozaar®	25 mg qd	50 mg ½ tab qd	\$291.12	Unscored teardrop shape
		50 mg qd	100 mg ½ tab qd	\$185.67	
	Benicar®	20 mg qd	40 mg ½ tab qd	\$267.36	Unscored
	Diovan®	80 mg qd	160 mg ½ tab qd	\$296.04	Unscored teardrop shape
		160 mg qd	320 mg ½ tab qd	\$252.40	
	Norvasc®	5 mg qd	10 mg ½ tab qd	\$181.66	Unscored
	Toprol XL®	25 mg qd	50 mg ½ tab qd	\$137.09	Scored†
50 mg qd		100 mg ½ tab qd	\$68.20		
Epilepsy Medications	Lamictal®	100 mg bid	200 mg ½ tab bid	\$1045.50	Scored
	Neurontin®	300 mg tid	600 mg ½ tab tid	\$213.63	Unscored
	gabapentin	300mg tid	600 mg ½ tab tid	\$72.92	Scored
	Topamax®	100 mg bid	200 mg ½ tab bid	\$1581.60	Unscored
	Trileptal®	300 mg bid	600 mg ½ tab bid	\$112.93	Scored
Erectile Dysfunction	Viagra®	50 mg	100 mg ½ tab	\$607.56	Unscored diamond shape††

\* Applies only to the tablet formulation. Capsules can't be split.

† Splitting is safe, even though Toprol XL® is an extended release formulation.

†† Assuming 10 doses dispensed monthly.

## Tablet Splitting *(continued from page 2)*

for tablet splitting. The Idaho Drug Information Service is available at (208) 282-4689 to answer any questions regarding tablet splitting potential of any medication not on the list.

Not all patients are good candidates for tablet splitting. Patient characteristics essential for successful pill splitting have been summarized in Figure 2. Patients should have the physical and mental capabilities to split tablets, and must be willing to do so. In one large trial that assessed compliance, pill splitting did not hinder compliance and only 4% felt it affected their willingness to take their medication.<sup>9</sup>

### Figure 2: Optimal Patient Characteristics for Good Tablet Splitting Outcomes

- Physical Ability
  - Avoid in patients with severe rheumatoid or osteoarthritis, multiple sclerosis, Parkinson's disease, or severe vision problems
- Mental Capacity
  - Avoid in patients with memory loss or severe mood disorders
  - Avoid in patients with alcoholism or psychosis
- Willingness
  - Patients should understand the rationale of tablet splitting and be willing to receive instruction in using a tablet splitter

The potential for confusion does exist. For example, "½ tablet" could be misinterpreted by the pharmacist or patient as "1-2 tablets," resulting in potential overdosage. Further, the patient may make assumptions that the pharmacist has either split or not split the tablets prior to receiving the prescription, resulting in potential over- or underdosage. Thus, it is essential that the prescription be written clearly and that the pharmacist clarifies and reinforces the physician's instructions with the patient.

The American Medical Association, the American Society of Consultant Pharmacists, the American Pharmaceutical Association, the National Association of Boards of

Pharmacy, and the Academy of Managed Care Pharmacy have all released position statements opposing mandated tablet splitting.<sup>10</sup> In fact, a class action suit has been brought against Kaiser for mandatory tablet splitting.<sup>2</sup> Voluntary splitting is a superior option, giving the physician the opportunity to evaluate each individual patient and medication for safety and appropriateness.

Many brand name medications cost the same per tablet regardless of strength. Ironically, pharmaceutical companies developed this pricing strategy precisely to avoid tablet splitting. However, the fact remains that pill splitting can result in cost savings of up to 50% when double-strength tablets are split in half – and this practice could save the state of Idaho hundreds of thousands of health care dollars annually.

Many of the drugs in Table Ib are prescription medications which can be split reasonably and safely while achieving significant cost savings. The economic rationale for prescribing many of these drugs in half tabs is compelling. The cost savings tend to overshadow the potential disadvantages as long as the medication and patient characteristics are carefully considered.

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## Cost Corner: Antidepressants and Suicidality

by Chris Owens, PharmD and Tracy Pettinger, PharmD

With the introduction of fluoxetine in 1988, a new era in the treatment of depression began. Since then, a variety of similar agents have been approved constituting a group of drugs commonly referred to as 'newer generation' antidepressants. These medications, including selective serotonin reuptake inhibitors (SSRIs) and some chemically unrelated agents (bupropion, venlafaxine, and mirtazapine) have largely replaced older pharmacologic treatment modalities in the management of major depressive disorder in both adults and children.<sup>1</sup>

Although often highly efficacious, antidepressant therapy is expensive with a monthly treatment course ranging from \$75-\$135. In 2003, Idaho Medicaid spent over \$14 million on antidepressants. Of note, the approval of therapeutically equivalent generics for many of these agents is likely to result in significant cost savings (see Table Ic). At the November 2004 Pharmacy & Therapeutics (P&T) Committee meeting for Idaho Medicaid, this class was discussed and due to high interpatient variability in response, it was decided that all drugs in this class would be given 'Medicaid preferred' status, although generics are required if available.

Recently, this class has come to the forefront of media attention and clinical debate because of an alleged increased risk of suicide, especially in pediatric patients. Because of this, a "black box" warning was added to the product labeling of all antidepressants in October 2004 (including MAOIs, TCAs, and SSRIs).<sup>2,3,4</sup>

Antidepressant-induced suicidality is poorly understood with much of the uncertainty attributed to the inherent

difficulty of demonstrating causality in a population clearly inclined toward suicide. One of the most agreed upon theories highlights the activating potential of antidepressants, which may give patients sufficient energy and drive to attempt suicide before the therapeutic benefits are fully realized.<sup>3,5</sup>

Table 1c: Comparison of Newer Antidepressants\*

Generic Name	Brand Name(s)	Typical Adult Dose	Cost* Brand	Cost* Generic
Bupropion	Wellbutrin	100mg TID	\$133.20	\$110.97
	Wellbutrin SR	150mg BID	\$123.97	\$94.59
	Wellbutrin XL	300mg QAM	\$116.18	N/A
Citalopram	Celexa	20mg QD	\$74.99	\$38.99
Escitalopram	Lexapro	10mg QD	\$66.60	N/A
Fluoxetine	Prozac	20mg QD	\$114.40	\$25.99
	Prozac Weekly	90mg Q WK	\$90.88	N/A
Fluvoxamine	Luvox	100mg BID	N/A	\$87.69
Mirtazapine	Remeron	30mg QHS	\$107.97	\$46.69
	Remeron SolTab	30mg QHS	\$95.97	\$87.97
Nefazodone	Serzone	200mg BID	N/A	\$39.69
Paroxetine	Paxil	20mg QD	\$87.48	\$73.39
	Paxil CR	25mg QAM	\$87.54	N/A
Sertraline	Zoloft	100mg QD	\$82.50	N/A
Venlafaxine	Effexor	75mg BID	\$113.40	N/A
	Effexor XR	150mg QD	\$102.26	N/A

\*Cost based on AWP for 30 day supply (at typical dosage) per 2004 Redbook

Randomized clinical trial data from depressed adults have revealed no convincing evidence that these medications increase suicide risk compared with placebo. The evidence is different for pediatric patients with an average risk of suicidality at nearly 4% (twice the placebo risk), although no suicides actually occurred in clinical trials.<sup>3,6</sup>

Although most evidence suggests that antidepressants do not increase suicidality in adults, evidence

from pediatric trials points to a small, but statistically significant increased risk. The FDA recommends increased monitoring of pediatric patients, especially upon initiation of one of these agents and with dosage changes. Ideally, weekly face-to-face contact with patients and/or family members is advised for the first 4 weeks, bi-weekly visits for the next 4 weeks, and as clinically indicated thereafter. Despite these recommendations and current media attention, it is also important to emphasize to patients that based on current information, untreated depression carries a far greater risk of suicide than does any antidepressant medication.

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## WHAT'S INSIDE!

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