



THERAPEUTICS INITIATIVE

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Pill splitting: Making the most of meds in a time of need

Clinical vignette

A 54 year-old mechanic with type 2 diabetes and hypertension had a myocardial infarction in 2015.

He currently takes ASA 81mg/d (over the counter) plus 6 generic prescription drugs dispensed monthly:

- atorvastatin 40mg/d
- ramipril 5mg/d
- empagliflozin 25mg/d
- escitalopram 10mg/d
- sildenafil 50mg 4 times/month
- duloxetine 90mg/d (60 mg + 30 mg)

He has been stable and working full-time but is concerned about potential drug shortages and costs, as he was just laid off. Hearing that splitting pills could save money, he bought a \$3 pill-splitter. During a Telehealth appointment (or call to your pharmacy) you realize that some of his pills could be prescribed at twice the dose per pill, but then split. This could save your patient unnecessary trips to the pharmacy, and precious dollars during the COVID-19 pandemic. A pharmacist can also recommend this. In the EMPA-REG trial, empagliflozin 10mg/d performed similarly to 25mg/d.¹ Dividing the 25mg pill to 12.5mg/d could halve the cost and extend supply. Duloxetine can't be split. But since it didn't help his back pain, you deprescribe by tapering his remaining supply.

Could tablet splitting help maintain drug supply during the pandemic?

The COVID-19 pandemic could affect pharmaceutical supplies, which were already subject to many shortages in Canada. Prudent prescribers, pharmacists and patients can help everyone get what they really need. This Letter covers basic information that may assist health professionals and the public to conserve medications wisely.

Twenty-five years ago, Therapeutics Letter #10 pointed out that we often prescribe larger doses than necessary to achieve intended pharmacological effects. We noted that larger 'recipe' doses increase the chance of adverse effects

as well as cost.² A 2018 study found that BC had Canada's highest rates of cost-related nonadherence due to prescription drug costs³, a national problem that greater affordability could address.

The Cochrane Hypertension Group has shown that much of the blood pressure lowering effect of antihypertensive drugs occurs at the lower end of the approved dose ranges.^{4,5} This applies to most if not all drugs used for high blood pressure. Statins also achieve most of their cholesterol lowering effect at the bottom end of their dose ranges. This is also generally true for analgesics, including acetaminophen, NSAIDs, opioids, gabapentin/pregabalin, duloxetine and tricyclics.⁶ Studies of antidepressants, antipsychotics, anxiolytics, sedatives, and many inhalers (including corticosteroids) show similar patterns.^{7,8} Official product monographs available by internet search often confirm that high doses are not superior to "low" doses.

For most preventive drugs we have no evidence about dose-response. Therapeutics Letter #87 concluded in 2013 that high dose statins are not clinically superior to lower doses.⁹ This has also been shown often for ASA (aspirin).

Pill splitting is one way to stretch prescriptions. This approach has been used to adjust doses for children, elderly or people with low body weight, and recommended previously both for safety and cost savings.¹⁰ Even rich societies with little previous incentive for cost containment may soon find this strategy appealing, if not compelling. People who check their own blood pressure or capillary glucose may be able to adjust some drugs to the intended targets (surrogate outcomes).

Dividing capsules is much harder. While many can be subdivided by a careful patient, this is not discussed here.



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Advantages of pill splitting

- reduce shortages by extending patients' medication supply;
- minimize trips to the pharmacy for refills, facilitating "social distancing";
- save money for patients and payers;
- improve medication adherence for people with financial barriers.

When not to split pills

- narrow therapeutic index, e.g. warfarin;
- full dose essential, e.g. anticoagulants, chemotherapy drugs, birth control pills, anti-seizure medications for epilepsy, corticosteroids for adrenal insufficiency or steroid-dependent patients;
- antibiotics and antivirals, unless advised by a professional;
- biologicals, for which we have little dose-response evidence;
- fragile pills that crumble easily.

When in doubt, patients should consult the prescriber or pharmacist.

Modified release tablets

Manufacturers and pharmacists typically warn against splitting enteric-coated or timed-release drugs (ER/CR/CD/SR/LA, etc). This may be overly conservative. For example, the TI has found no scientific reason why splitting a proton pump inhibitor (PPI) will prevent it from suppressing stomach acid. Swallowing a fragment with a full glass of water assists absorption. Timed-release drugs often have a relatively wide intrinsic range of peak concentration (C_{max}) and time to peak (T_{max}). If a sudden peak could cause profound sedation, low blood pressure, or respiratory depression, splitting the dose may not be safe. Drugs intended for delivery to the large bowel such as 5-ASA (Asacol) or controlled release L-DOPA (Sinemet CR) typically should not be split.

Pill splitting is not for everyone

Pill-splitting may be inappropriate for people with unstable, complicated or dangerous conditions. The most responsible prescriber(s) should determine safety of any possible changes. For people with serious psychiatric conditions, a prescriber who knows the patient should be consulted.

What is the evidence on the benefits and safety of pill splitting?

BC's modest pill splitting record could easily be improved. In 2006, splitting only 2.6% of statin prescriptions saved an estimated \$2.3 million. People with low incomes and women tended to take advantage of this strategy.¹¹

A 2012 review of tablet splitting studies (statins, antihypertensives and one antipsychotic) suggested that cost savings can be achieved without adverse clinical outcomes.¹²

A 2015 CADTH review¹³ assessed clinical and cost effectiveness and found one guideline, from the Liverpool Children's Hospital. For hospitalized patients, this recommended using a pill-splitter along the tablet scoreline, and not < ¼ segments.

Can a "drug holiday" or deprescribing be considered?

At any careful medication review, it is worth considering a "drug holiday" (temporary deprescribing) or permanent deprescribing.

Writing the prescription

Communicate clearly and unambiguously. Partial example for case vignette:

1. Atorvastatin 80mg tablets. Dispense 45 to last 90d.
Take ½ = 40mg daily for secondary prevention of IHD.
2. Empagliflozin 25mg tablets. Dispense 45 to last 90d.
Take ½ = 12.5mg daily to prevent complications of type 2 diabetes.
3. Escitalopram 20mg tablets. Dispense 45 to last 90d.
Take ½ = 10mg daily for depression.
4. STOP duloxetine (patient will taper his remaining supply).

Conclusions

- **Consider deprescribing. Does this patient really need this medication?** Could one try stopping it?
- **Consider pill splitting to stretch prescriptions and save money.** This may assist social distancing or quarantine, and extend drug supplies. Halving the dose can work well for many indications. Splitting a larger pill can maintain dose at lower cost.
- Some drugs, e.g. anticoagulants ("blood thinners") should not be split.
- Patients considering this strategy should talk with their prescriber or dispensing pharmacist, if possible.

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Table: Potential savings from Rx pill splitting (vignette)

Some branded drugs cost much more (e.g. Lipitor, Altace, Cipralex)

BC prices based on BC PharmaCare April 1, 2020 Low Cost Alternative Program*

Drug and dose (generics only)	Unit cost**	Approximate annual savings by splitting higher dose tablet
atorvastatin 80mg	≈ \$0.25	
½ x 80mg = 40mg	≈ \$0.125	\$45.6
atorvastatin 40mg	≈ \$0.25	
ramipril 10mg	≈ \$0.11	
½ x 10mg = 5mg	≈ \$0.055	\$12
ramipril 5mg	≈ \$0.088	
empagliflozin 25mg	≈ \$2.96	
½ x 25mg = 12.5mg	≈ \$1.48	\$540
empagliflozin 10mg	≈ \$2.96	
escitalopram 20mg	≈ \$0.36	
½ x 20mg = 10mg	≈ \$0.18	\$58.4
escitalopram 10mg	≈ \$0.34	
sildenafil 100mg	≈ \$3.18	
½ x 100mg = 50mg @ 48/y	≈ \$1.59	\$70.6
sildenafil 50mg	≈ \$3.06	
duloxetine 60mg	≈ \$1.05	<i>not practical to split</i>
duloxetine 30mg	≈ \$0.52	\$573 by stopping both

Total possible savings from splitting 5, deprescribing 1 drug: ≈ \$1300
(Substituting generic for brand name drugs could save more)

* <https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/how-pharmacare-covers-drugs-in-the-low-cost-alternative-lca-program>

** maximum reimbursed by BC PharmaCare; pharmacies may charge more





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