PHARMACIST'S LETTER

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PRESCRIBER'S LETTER

Common Oral Medications that May Need Tapering

Tapering to prevent a withdrawal syndrome or disease state worsening is suggested for several medications. The chart below provides suggested tapering strategies for some common oral medications. For some medications, more than one tapering method has been proposed, and the best approach is unknown. Evidence is mostly anecdotal, and a more cautious approach may be needed in certain patients (e.g., high dose, long treatment duration, severe disease). Educate patients and caregivers for which symptoms they should alert the prescriber or seek emergency treatment. Reassure and offer symptomatic relief for milder symptoms. Cognitive behavioral therapy may be needed in some situations (e.g., benzodiazepine withdrawal). It has been suggested that medication dose reduction of 25% at weekly or longer intervals, with patient monitoring, is a reasonable approach to tapering in general. When considering a timeline for tapering, take into account the patient's age, comorbidities, concomitant medications, medication half-life, reason for taper (e.g., side effects), and consequences of withdrawal.[1]

NOTE: Information in chart may differ from product labeling. Information from Canadian labeling is included when it differs significantly (e.g., more conservative) from referenced U.S. labeling.

Drug or Drug Class	Rationale for Taper	Suggested Taper
Antidepressants *Continued…*	Withdrawal symptoms (FINISH syndrome): Flu-like symptoms, Insomnia, Imbalance, Sensory disturbances, Hyperarousal.[2] Symptoms usually begin & peak within one week, last one day to three weeks, & are usually mild.[2] Most common with paroxetine (*Paxil*) & venlafaxine (*Effexor*).[3]	All antidepressants should be tapered except perhaps fluoxetine (*Prozac*), which has a long half-life.[3,4] Taper over at least four weeks if taken for at least six weeks.[13] Canada: taper venlafaxine ER if used more than one week.[14] Consider more prudent approach (e.g., for paroxetine, venlafaxine) of reducing dose by 25% every four to six weeks.[4] Reduce the daily dose of venlafaxine ER by 37.5 to 75 mg weekly or paroxetine CR by 12.5 mg weekly.[15,16,59] Limited dosing strengths may present challenges for gradual dose reduction for some antidepressants. Consider these tips: • Desvenlafaxine: consider extending the dosing interval.[59] In the U.S., a desvenlafaxine 25 mg extended-release tablet is available to facilitate tapering. • Duloxetine: in clinical trials, dose was reduced in two steps.[59] • Venlafaxine: discontinue once a daily dose of 25 or 37.5 mg is reached.[59] Tapering may not completely eliminate symptoms.[2] Educate patients symptoms are usually transient and mild. If symptoms are problematic, return to previous dose or switch to fluoxetine.[3]

More. . .

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Drug or Drug Class	Rationale for Taper	Suggested Taper
Antidepressants, continued		In acute bipolar mania taper over three to five days.[12] In panic disorder, reduce by one dosage step every one to two months.[42] In obsessive compulsive disorder, reduce by 10% to 25% every one to two months.[43] See our *PL Chart, Choosing and Switching Antidepressants*, for information on tapering in the context of switching.
Anticonvulsants	Recurrence or worsening of condition being treated or comorbidities (e.g., seizures, mood disorder, headache).[5] Gabapentin or pregabalin withdrawal symptoms: anxiety, insomnia, nausea, sweating, pain, irritability, agitation, akathisia, palpitations, diarrhea, headache, flu-like symptoms, increased blood pressure, weakness, mental status changes, catatonia, seizures.[6,8,11,52] There is at a case of status epilepticus in a patient without a seizure history withdrawn abruptly from gabapentin 8000 mg/day.[62]	Taking into account safety, quality of life, and lack of evidence, a relatively rapid taper (one to three months) has been suggested in patients with epilepsy. Most seizures occur in the first six months after withdrawal, so a slower taper prolongs the "at risk" relapse period.[5] Taper gabapentin or pregabalin over at least one week.[6,9,11] Some patients (e.g., those with seizures) may need tapered over weeks or months.[5,52] Migraine prophylaxis: consider 25% (of original dose) dose reduction weekly or monthly.[7] Bipolar disorder: taper over at least two to four weeks.[12]
Antipsychotics *Continued…*	Recurrence of neuropsychiatric symptoms.[13] Withdrawal symptoms (best-documented with clozapine): sweating, salivation, runny nose, flu-like symptoms, paresthesia, bronchoconstriction, urination, gastrointestinal symptoms, anorexia, vertigo, insomnia, agitation,	No more than 50% every 2 weeks.[19] Abrupt discontinuation can be appropriate in the hospital setting.[17] If switching to a different antipsychotic, most experts suggest cross-tapering: reducing the dose of the old antipsychotic while uptitrating the new antipsychotic at about the same rate (e.g., over two to three weeks).[18,20] Consider starting with the usual initial dose of the new agent and continuing it for at least a week before uptitrating, while tapering the old medication over several weeks.[21] OR

Drug or Drug Class	Rationale for Taper	Suggested Taper
Antipsychotics, continued	anxiety, restlessness, movement disorders, psychosis.[17,18]	• Wait to begin tapering the first agent until the new agent is uptitrated to a therapeutic dose (i.e., plateau cross-taper).[23] This method is the most effective for preventing relapse, but has the highest risk of adverse effects and drug interactions.[24] The product labeling for some antipsychotics, particularly long-acting injectable formulations, provide switching guidance.
Baclofen	Worsening of spasticity, or withdrawal symptoms: delirium, hallucinations, confusion, seizures, movement disorders, psychosis, paranoia, mania, anxiety, tachycardia, sweating, insomnia.[25]	Taper over about one to two weeks.[25]
Benzodiazepines (Also, included in this section are the Benzodiazepine Receptor Agonists or "Z drugs" [e.g., eszopiclone, zolpidem, zaleplon, and zopiclone].)	Relapse or rebound of condition being treated; withdrawal symptoms: sweating, tachycardia, muscle cramps, tremor, insomnia, anxiety, agitation, nausea, vomiting, hallucinations, seizures.[10,34] Risk factors for withdrawal: use over one year, high dose, short duration of action (e.g., triazolam [*Halcion*], alprazolam [*Xanax*; especially if daily dose >4 mg for >12 weeks], lorazepam [*Ativan*]).[10,27,28,34]	**Benzodiazepines**: Consider reducing the dose rather than extending the dosing interval to avoid between-dose withdrawal.[26] Consider using liquid formulations for small doses.[22] In panic disorder, discontinue over two to seven months, at a rate not more than 10% per week.[42,44] "**Z drugs**" (e.g., eszopiclone [U.S.], zolpidem, zaleplon [U.S.], zopiclone [Canada]) may need to be tapered (or replaced with a long-acting benzodiazepine, which is then tapered) in patients who have escalated the dose.[53,54] Product labeling for these drugs suggests that when taken as directed, withdrawal symptoms are uncommon and not serious. Nevertheless, Canadian labeling for zolpidem and zopiclone recommends tapering in patients taking the drug for more than a few weeks.[55-57] Suggested approaches to discontinuing "Z drugs" include: • substituting another sleep medication (e.g., melatonin, trazodone, mirtazapine)[58] • taper to lowest effective dose, then gradually eliminate doses. Takes about eight weeks for patients who take Z drugs nightly.[61] • switching to lorazepam and tapering by 10% to 25% per week, or 10% every two to four weeks, depending on reason for discontinuation.[58] See our *PL Chart*, *Benzodiazepine Toolbox*, for other tips for tapering oral benzodiazepines.

Drug or Drug Class	Rationale for Taper	Suggested Taper
Beta-blockers	Sudden withdrawal has been associated with angina, myocardial infarction, and arrhythmias in patients with coronary artery disease.[30] In patients without coronary artery disease, only mild, short-lived withdrawal symptoms such as anxiety or tachycardia may be seen, but angina and myocardial infarction have been reported.[31] Hypertensive urgency has been reported.[29] It is prudent to taper beta-blockers over about a week even in patients without overt coronary artery disease.[30]	Taper over one to two weeks.[29] If withdrawal symptoms occur, reinstate therapy, at least temporarily.[30]
Butalbital combination products (e.g., *Fiorinal*)	Headache exacerbation, tremors, delirium, seizures.[32] Risk factors: continuous, long-term use of seven or more doses daily.[32]	Taper over four to six weeks. If patient taking 12 or more doses daily, consider referral to specialist.[32]
Calcium Channel Blockers	Exacerbation of angina.[40]	No specific taper suggested.
Carisoprodol	Body aches, sweating, palpitations, sadness, anxiety, restlessness, insomnia.[33]	Long taper (for patients with renal or liver impairment, age >65 years, or total daily dose >1400 mg): 350 mg three times daily for three days, then twice daily for three days, then once daily for three days.[33] Short taper: 350 mg three times daily for one day, then twice daily for two days, then once daily for one day.[33]

Drug or Drug Class	Rationale for Taper	Suggested Taper
Cholinesterase inhibitors (e.g., donepezil)	Discontinuation syndrome: labile mood, agitation, insomnia, trouble concentrating.	Reduce donepezil dose to 5 mg once daily for four weeks, then stop.[45] Monitor closely and restart quickly in the event of deterioration.[49]
Clonidine	Withdrawal syndrome: rebound hypertension, headache, restlessness, anxiety, insomnia, sweating, tachycardia, tremor, muscle cramps, hiccups, nausea, salivation; rarely encephalopathy, stroke, death.[35] Risk factors: use for over one month, concomitant beta-blocker use, daily dose >1.2 mg daily, hypertension, cardiovascular disease.[35]	Taper over one to two weeks[64] (e.g., 0.1 mg every three to seven days).[35,63] Beta-blockers increase risk of rebound hypertension during clonidine withdrawal (noncardioselective most problematic [e.g., propranolol]). If patient is also taking a beta-blocker, consider taper of beta-blocker first. Monitor BP closely after clonidine taper.[60] Transdermal: Risk of withdrawal lower than with oral, but consider tapering patches over two to four days or switching to oral clonidine taper.[35]
Corticosteroids	Adrenal insufficiency or worsening of underlying condition.[36]	See our *PL Chart*, *Using Oral Corticosteroids: a Toolbox*.
Guanfacine (*Tenex*, generics)	Catecholamine rebound: anxiety, nervousness, transient increase in blood pressure higher than pretreatment level (less problematic than with clonidine).[37] Risk factor: higher doses.[37]	Taper over one to two weeks[64] (e.g., 1 mg every three to seven days).[65]
H2 Blockers	Acid rebound.[38]	No specific taper suggested.
Memantine (e.g., *Namenda*)	Discontinuation syndrome: insomnia, aggression, delusions, disinhibition.[48]	No specific taper suggested. Concern that symptoms may not be fully reversible if there is a delay in restarting pharmacotherapy if symptoms occur.[48]
Nitrates	Rebound angina.[35]	Not usually tapered, but consider tapering over one to two weeks with sublingual nitroglycerin as needed.[35]

Drug or Drug Class	Rationale for Taper	Suggested Taper
Opioids	Withdrawal symptoms: flu-like symptoms, insomnia, anxiety, abdominal cramps and other GI symptoms, goose bumps, fatigue, malaise.[46]	See our *PL Chart, Opioid Discontinuation: FAQs*, for tips.
Parkinson's disease medications (dopaminergic drugs)	Withdrawal syndrome resembling neuroleptic malignant syndrome.[38]	Taper over about four weeks.[38]
Proton Pump Inhibitors	Rebound acid secretion.[38]	Taper over four to six weeks. Reduce dose every week or two. Once lowest dose is reached, take it every other day for a week or more. Can further increase the interval to every third day, etc. Consider stepping down to an H2 blocker.[41]
Tapentadol (*Nucynta* [U.S.], *Nucynta IR* [Canada], *Nucynta ER* [U.S.], *Nucynta CR* [Canada])	Withdrawal symptoms: anxiety, insomnia, tremors, rigors, pain, nausea, diarrhea, upper respiratory symptoms, sweating, goose bumps, and rarely hallucinations.[39]	No specific taper suggested.
Tizanidine (*Zanaflex*)	Withdrawal symptoms: rebound hypertension, tachycardia, hypertonia.[47] Risk factors for withdrawal symptoms: daily dose ≥20 mg, use for nine weeks or more, concomitant opioid use.[47]	Decrease dose by 2 to 4 mg each day.[47] Tapered over one week in clinical trials.[47]
Tramadol (*Ultram*, etc).	Withdrawal symptoms: anxiety, restlessness, insomnia, sweating, goose bumps, rigors, pain, nausea, tremors, diarrhea, upper respiratory symptoms, hallucinations (rarely), panic attacks, paresthesias, autonomic dysfunction, abdominal cramps, migraine-like headaches, myoclonus, and restless legs syndrome.[50,51]	No specific taper suggested.
Z Drugs	See "Benzodiazepines," above.	

Users of this PL Detail-Document are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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