

Hospice Medication Deprescribing Toolkit

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Introduction

The NHPCO Hospice Medication Deprescribing Toolkit was created as a companion resource to the NHPCO Medication Flow Chart – Determination of Hospice Medication Coverage, developed by the myNHPCO Pharmacist Community and released in April 2020. Decision trees in the flow chart describe opportunities for deprescribing medications at the end of life. This collection of independent deprescribing guidance documents can assist hospice agencies when evaluating if medications could be continued or deprescribed.

This toolkit is made available by the myNHPCO Pharmacist Community in collaboration with the myNHPCO Physician/Advanced Practice Provider Community and numerous hospice professionals. The following individuals are recognized for their effort in the development of this toolkit.

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Disclaimer

All clinical recommendations contained herein are intended to assist with determining the appropriate therapy for the patient. Responsibility for final decisions and actions related to care of specific patients shall remain the obligation of the institution, its staff, and the patients attending physicians. Nothing in this document shall be deemed to constitute the providing of medical care or the diagnosis of any medical condition. Use of product brand names are intended to assist the clinician in identifying products and does not connote endorsement or promotion of any kind. No financial support for the development of this toolkit was provided by any product, vendor, or manufacturer.

Are Your Patient's Pills a Burden? Discussing Polypharmacy with Patients

Pill Burden and its Impact on Patients¹⁻³

Pill burden describes how taking medications can place challenges or inconveniences on someone's life. Polypharmacy, or taking more than 3-5 medications per day, is the main contributor to pill burden for most patients. Challenges include:

Complicated medication routines: Taking multiple medications, multiple times per day. For example, most patients taking more than 3 or 4 medications will require at least twice a day dosing. Each additional medication increases the complexity of the daily pill-taking regimen. More than one prescriber or using more than one pharmacy adds even more burden and risk to the medication use process. Unless prescription pick-up times are synchronized at a single pharmacy, that also means repeated visits to the pharmacy for medication refills. If someone has multiple prescribers, then the likelihood that each prescriber and the pharmacy have an accurate and complete list of all of medications is low. When patients self-select over-the-counter (OTC) medications and natural or herbal products, they may forget to inform their healthcare team.

Medication characteristics: Medications may look very different in size and shape. With generic medication substitutions at the pharmacy, the appearance of a medication may change at the time of refills. People with multiple medical issues may need to take multiple forms of medications – injections for diabetes, pills for cardiovascular disease, transdermal patches for pain, and inhalers for COPD. Inhalers are a particular challenge because each type of inhaler has different instructions for use. If the patient has any level of cognitive impairment, the risk of potentially harmful medication errors can greatly increase.

Medication adverse effects: The more medications a patient takes, the higher the risk of drug interactions and drug side effects. Side effects can sometimes be so troublesome for patients that they stop taking the medication and risk worsening of their health condition. Medication side effects can lead to polypharmacy (known as a prescribing cascade) when those side effects are managed by adding another medication. In the case of using laxatives to manage the constipation from opioids, the addition is necessary because the opioid is needed to control pain; the side effect of constipation will not lessen over time and must be managed for the comfort of the patient. However, using a medication for incontinence, a common side effect of medications for dementia like donepezil (Aricept®) may improve incontinence but can actually worsen cognition and lead to dry mouth and constipation as well.

Social and family impact: As patients become more frail and reliant on family members for support, pill burden begins to impact family caregivers as well. Depending on patient health insurance coverage and the rising price of prescription medications, the financial impact can strain the family budget.

Tips for Reducing Polypharmacy and Pill Burden⁴⁻⁷

Keep patient-centered care aimed at improving quality of life as the focus of both interdisciplinary team (IDT) meetings and patient-family discussions; target symptom improvement over changes in lab values. Reduction in polypharmacy often leads to improvements patient-reported wellbeing without significant adverse reactions. See Figure 1 for an example of a de-prescribing algorithm.

If patients are non-adherent to their prescribed medications, ask if they are concerned about side effects, tired of taking so many medications, or how well they feel the medications are helping to manage their symptoms.

Reassess each medication for ongoing indication and need. In hospice, if a medication is intended for disease prevention rather than palliating a symptom, consider tapering and discontinuing the medication.

Engage other IDT members to assist managing symptoms such as pain or dyspnea. Hospice social worker, spiritual care counselor, and other therapists can help plan non-pharmacologic interventions to help manage symptoms without adding to pill burden.

If possible, use once daily or twice daily dosing options instead of multiple daily doses. Optimize the dose of long-acting pain medications so the patient doesn't need to rely on multiple breakthrough doses to control pain.

Figure 1. Garfinkel De-prescribing Algorithm⁷

Discuss the following with the patient/guardian



Algorithm adapted from: Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults. Arch Intern Med 2010;170(18):1648-1654

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ANTIPLATELET & ANTICOAGULANT MEDICATIONS

Antiplatelet & Anticoagulant Medications DEPRESCRIBING GUIDANCE



Background

Many patients are admitted to hospice services already taking an antiplatelet or anticoagulant medication, especially if they have cardiovascular disease or a history of blood clots due to cancer. A recent study reported the prevalence of antithrombotic therapy at the time of hospice enrollment at nearly 7% of patients, with about 57% of those patients on aspirin therapy and over 18% on multiple antithrombotic medications.¹

Antiplatelet medications prevent blood clots by inhibiting platelet aggregation and are used to decrease the risk of death from cardiovascular events such as myocardial infarction (MI), ischemic stroke, angina, or peripheral arterial disease.² Aspirin is the original antiplatelet medication, and is available over-the-counter (OTC); patients may choose to take aspirin without prescriber advice. Non-aspirin antiplatelet medications are also used off-label for secondary prevention of cardiovascular disease in patients with diabetes or aspirin allergy, and in some patients with atrial fibrillation to prevent thromboembolism.² Additionally, clopidogrel or prasugrel may be used in dual antiplatelet therapy (DAPT) in combination with aspirin for patients with acute coronary syndrome (ACS) or following stent placement.²

Anticoagulant medications also prevent blood clots but instead of inhibiting platelets, they prevent blood coagulation by reducing the action of clotting factors directly or indirectly. Anticoagulants are also used to prevent clotting in patients with atrial fibrillation, thromboembolic disease, and artificial heart valves.²

TABLE 1 – ANTIPLATELET AND ANTICOAGULANT MEDICATIONS						
Antiplatelet Medications						
Aspirin	Clopidogrel	Tiagrelor	Prasugrel	Aspirin-		
	(Plavix®)	(Brilinta®)	(Effient®)	Dipyridamole		
				(Aggrenox®)		
Anticoagulant Medications						
Warfarin	Apixaban	Rivaroxaban	Dabigatran	Enoxaparin	Edoxaban	
(Coumadin®)	(Eliquis®)	(Xarelto®)	(Pradaxa®)	(Lovenox [®])	(Savaysa®)	

The decision to discontinue antiplatelet and anticoagulant medications should always be an individualized approach, weighing the risks vs benefits, and the patient and family's goals of care. Discontinuing these medications is generally considered acceptable in any patient with a life-limiting illness, especially when adverse effects are possible.³ The information below is based on literature review in the primary care and hospitalized patient population; there are no studies determining risk vs benefit of aspirin, other anti-platelet therapies, or anticoagulants for patients in hospice or palliative care. Due to the likelihood of drug interactions, consulting with a pharmacist when adding or discontinuing any medication is recommended.

Why Deprescribe?

CONSIDER DEPRESCRIBING IF ANY OF THE FOLLOWING FACTORS IS PRESENT:						
	Patient at risk for bleeding	 Increased risk for major hemorrhage or bleeding complications present in patients on anticoagulation therapy with advanced age, CHF, CVD, hypertension, liver or renal disease, diabetes, history of or recent GI bleed, anemia, concomitant use of antiplatelets or NSAIDs.^{6,8,11,12} HAS-BLED score tool can be used to assist clinicians in identifying patients at high risk for bleeding.⁷ When bleeding does occur, lack of access to reversal agents other than vitamin K (phytonadione) can be difficult. Hospitalization is required for patients to use the reversal agents for dabigatran, apixaban, and rivaroxaban to manage bleeding.² 				
		No palliative benefit present or clinical sians of impending death				
	Medication may no longer be indicated	 Antiplatelet or anticoagulant medications may have been started with time-limited intent after a procedure or event. Evaluate continued need and potential to de-escalate to aspirin monotherapy or deprescribe entirely. Benefits of multiple antiplatelet or anticoagulation combination therapy is generally limited to 3-12 months of therapy; likely no additional benefit to longer therapy, only increased risk of ble diagona service in the base is a service of the servic				
	Patient at risk for falls	 Hospice patients, young and old, have an increased risk of falling, and potential for internal or external bleeds. Risk of an intracranial hemorrhage in a debilitated ambulatory patient who may fall is greater than the benefit in preventing a stroke.⁵ 				
	Patient at risk for drug- drug interactions	 Drug interactions are common with these classes of medications (especially warfarin) increasing bleeding risk or increased clot formation.² Device and institute and increased in the and arrest in the and increasing bleeding risk or increased in the and arrest in the arrest in the				
		Review medication profile with a pharmacist when adding or discontinuing any medications.				
	Decreased renal or hepatic function	 Many of antiplatelet and anticoagulant medications rely on liver metabolism and renal clearance.² Bleeding increases with kidney or liver impairment, especially in elderly patients. Avoid warfarin in patients with liver failure.⁵ 				
	Decreased nutritional intake	 Hospice patients may have fluctuating nutritional intake, impacting vitamin K intake and affecting the therapeutic risk/benefit associated with warfarin. Warfarin, rivaroxaban, and apixaban are highly protein bound anticoagulants. Malnourished patients with low albumin are at an increased risk of bleeding due to higher than usual exposure to circulating active drug.² 				
	Difficulty swallowing	Dabigatran must be swallowed whole; crushing results in excessive absorption and toxicity. ² Deprescribe if patient cannot swallow intact tablets.				
	Increase in pill burden and frequent monitoring	 Antiplatelet and anticoagulant medications contribute to polypharmacy and pill burden. Warfarin requires routine PT/INR testing. Patients may wish to avoid finger sticks or blood draws. If routine bloodwork or INR testing is refused by patient/family, discontinue warfarin.⁵ 				
	Continued use is outside the goals of care	Continuing medications that are not relieving any symptoms (i.e. not palliative), may be outside the goals of care (exception may be treatment of DVT).				

Patient & Caregiver Talking Points

The BUILD Model provides a structured process to discuss deprescribing with patients, family, and caregivers.⁹ The basics of the BUILD mnemonic and sample conversational phrases for family and caregiver discussions are below.

BUILD	UNDERSTAND	INFORM	LISTEN	DEVELOP
A foundation of trust and respect	What the family knows about the device	The family about clinical evidence	To the family's goals and expectations	A plan of care in collaboration with family

Acknowledge that patient and family concern about medication changes, especially stopping medications is common response.

Provide reassurance that all medication changes are made in consultation with the patient's doctors. The decision to stop antiplatelet and anticoagulant medications is always an individualized approach.

Ask the patient and family questions to bring them into the shared decision-making process. Use open ended questions that lead into conversations about stopping medications.

— "Do you know why you are taking this medication? Is it hard to take all these pills every day? Do you ever feel worse after taking this pill? Have you noticed your wife is eating less than she used to? Have you felt unsteady when walking lately? Are you worried about your mom falling? What are your goals now that your dad is on hospice?"

Explain that as patients age or diseases progress, certain medications that were once helpful can become harmful. The hospice team's role is to enhance comfort and quality of life by providing effective and safe medications, treating physical and emotional symptoms, and minimizing adverse events.

- "Dr. Jones would like to discuss stopping your wife's warfarin. Since you shared that she is no longer eating much and has fallen a few times over the past month, he is concerned the medication is no longer safe for her to take. The risk of her developing a bleed in her brain or stomach is greater than the risk of her having a stroke over that same time frame.

Remind the patient and family that the hospice team will regularly reassess the patient's condition and medications

— If the patient has a relatively good prognosis, has a symptomatic DVT or is at high risk for thromboembolism, is still ambulatory, adherent to their prescribed medication regimen, and at low risk for bleeding, the patient may benefit from continued anticoagulation. Reassess at each visit, change in condition, or change in location of care to determine continued need for the medication.

- For some patients following ischemic stroke, MI, stents, or other cardiovascular event, the risk of a second event may outweigh the risk of a GI bleed, indicating that continuing the medication is reasonable.

Sometimes changing to an alternative, potentially safer medication is an option to meet the patient and family halfway

— For example, aspirin seems to be similar in effectiveness to clopidogrel for patients with a history of cardiovascular or stroke; for patients wanting to continue some antiplatelet therapy, a change to aspirin can be considered. DAPT does not have significant benefit over aspirin alone for secondary prevention of MI or stroke.⁴

How to Deprescribe

Once the decision has been made to discontinue antiplatelet or anticoagulant medications, they may be stopped without a taper.

If family or patient is hesitant to discontinue, consider a trial discontinuation for a limited period of time (e.g., 2 weeks or 1 month) and offer to re-evaluate once that trial is completed. Often, the family or patient needs this time as an "adjustment period" to accept the possibility of discontinuation, understand the medication is not helping, and realize that continuation is not necessary.

References & Additional Resources

Additional Resources

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DEMENTIA MEDICATIONS

Dementia Medications DEPRESCRIBING GUIDANCE



Background

The role of acetylcholinesterase inhibitors (AChEI) and memantine (Table 1) in terminal dementia has been somewhat controversial for more than a decade. In a 2009 survey of hospice medical directors, 80% recommended deprescribing them, but a minority felt there was continued benefit.¹ Clinical guidelines and medical texts have since evolved to consider deprescribing these drugs, but there is still no universal consensus.²⁻³ Even when clinicians determine that deprescribing is warranted, they are likely to encounter significant resistance from family and caregivers who commonly report negative feelings and apprehension about the process.¹⁻⁴

	TABLE 1 – DEMENTIA MEDICATIONS	
Acetylcholinesterase inhibitors (AChEl)	NMDA receptor antagonist	Combination products
donepezil (Aricept®)	memantine (Namenda®)	memantine and donepezil (Namzaric®)
rivastigmine (Exelon®)		
galantamine (Razadyne®)		

Why Deprescribe?

Clinical practice guidelines are a primary way in which providers practice evidence-based medicine. A recent review found that more than two-thirds of guidelines advised AChEl deprescribing under certain conditions.⁶ Guidelines that recommend deprescribing and their rationale for doing so are listed in Table 2.⁵

	TABLE 2 – GUIDELINE-CITED REASONS F		IEI DEPR	ESCRIBI	NG⁵			
0	1 Lack of Response / Loss of Effectiveness – can be difficult to gauge, so ask the caregiver and/or original prescriber guestions like "When the drug was started, do you feel like it helped?" or "Do you feel like the drug is still helping?"							
2	 Adverse Effects – generally due to AChEI-induced excess cholinergic activity; includes diarrhea, nausea/vomiting, bradycardia, bronchospasm, incontinence, weight loss, peptic ulcer disease. Deprescribe AChEI if adverse effects are intolerable 							
3	Severity of Cognitive / Functional Impairment – e.g., Mini Me sessment Staging Test (FAST) score worse than 7A	ntal Sta	te Examir	nation sco	ore < 10 or	- Functior	nal As-	
4	Institutionalization - i.e., no longer a need to prevent institut	ionalizat	tion if cur	rently inst	titutionali	zed		
6	Medical Status – e.g., terminally ill, actively dying, new fractu	re, infec	tion					
6	Family / Caregiver / Patient Preference – always deprescribe	AChEl i	f this grou	up agrees	to do so			
	Guideline Sponsoring Organization (Year) & Rationale for Deprescribing	1	2	3	4	5	6	
Amer	ican Academy of Family Physicians (2011)	~						
Amer	ican Geriatric Society (2014, 2015)	~					~	
Britis	h Association for Psychopharmacology (2017)					~		
Britis	h Psychological Society & Royal College of Psychiatrists (2007)	~		~				
Canao Deme	Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (2014)							
Califo Mana	California Workgroup on Guidelines for Alzheimer's Disease Management (2011)							
Singa	Singapore Ministry of Health (2013)						v	
Natio	nal Institute for Health and Care Excellence (2016)	~		~				
Prima	Primary Health Tasmania (2016)							

V

World Federation of Societies of Biological Psychiatry (2011)

~

Additional reasons to deprescribe AChEl include:

Drug-drug / drug-disease interactions – AChEl are pro-cholinergic and may blunt the intended effects of anticholinergic medications [e.g., ipratropium (Atrovent®), glycopyrrolate (Robinul®), tiotropium (Spiriva®)]. AChEl prescribing information warns against use in patients with medical conditions like bradyarrhythmia, lung disease, and peptic ulcer disease.

Inconsistent adherence – discontinue AChEl in patients who are unable or unwilling to take regularly.

Dysphagia – Loss of swallowing ability should prompt a deprescribing discussion before switching routes of administration (oral tablets to transdermal patches) or crushing tablets, or changing to liquid formulations or rectal administration. Proactive deprescribing with a planned taper may help avoid withdrawal symptoms in the future (see How to Deprescribe below).

Like AChEI, memantine is a candidate for deprescribing. While patients receiving memantine are less likely to discontinue due to problematic side effects compared to AChEI, a recent meta-analysis determined memantine to have limited effectiveness for dementia symptoms.⁶ Memantine is not effective in mild to moderate dementia⁷ and the Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail) recommends a trial of deprescribing in patients with moderate-severe dementia who are frail or have a limited life expectancy.⁸

Patient & Caregiver Talking Points

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Acknowledge the family's concerns about discontinuing medications for dementia. Use language that allows the family time to process the discussion while encouraging continued thought and a return to the conversation at a future visit.

Adverse drug events, bothersome side effects, and transitions in location of care require a more direct discussion and medication profile review. These are good opportunities to discuss discontinuing medications to reduce pill burden and preserve quality of life.

Bring the family into a shared decision-making process by developing the plan of care with them. Ask them about their expectations for the dementia medications, what they have noted as far as benefit or side effects, and recognize the support and care they have provided for months and years prior to the start of hospice care.

— "We understand this can be stressful and you may have fears, worries or feel guilty stopping these medications. If you're not ready right now, let's plan to talk about it again later."

- "Stopping the drugs can be done on a trial basis ("drug holiday"). The hospice team will carefully monitor the process and collaborate with the facility staff. If we see any concerns, we can always pause the taper or restart the Exelon."

- "Our goal is to provide comfort, but your mom's Aricept seems to be causing her more problems now and her ability to recognize her family and her agitation seems to be getting worse lately. Are you noticing this too?"

— "While on the Namzaric for dementia your father's dementia has gotten worse. We think the medication has provided all the benefit it can. In other words, the Namzaric did their job and he was able to stay home a few more months before moving to long-term care."

How to Deprescribe

Deprescribing guidelines typically recommend a tapered discontinuation, when possible, to reduce risk of withdrawal symptoms that may occur after abrupt withdrawal. Tapering schedules of up to 50% per week over 2-4 weeks have been proposed, especially after long-term use.^{2,10,11}

AChEI discontinuation syndromes have been reported but usually in patients with mild to moderate dementia.^{2,10,12-14} Dementia's effects on individual patients are inherently unpredictable; changes following discontinuation may not be related to deprescribing. Case reports of clinical deterioration describe changes following discontinuation. A meta-analysis found the rate of cognitive decline to occur in the 6 weeks following discontinuation.² Patients with baseline psychosis may be more prone to decline.¹⁰ New onset of agitation, anxiety, delirium, tearfulness, mood changes, insomnia, or paralytic ileus that are reasonably attributed to AChEI withdrawal should prompt an evaluation that considers AChEI reintroduction, or if a AChEI taper is still in progress, to taper at a slower rate.¹²⁻¹⁴

References & Additional Resources

Additional Resources

Deprescribing.org – Cholinesterase Inhibitor (ChEI) and Memantine Deprescribing Algorithm, https://cdpc.sydney. edu.au/wp-content/uploads/2019/06/algorithm-for-deprescribing.pdf

PHN Tasmania – A Guide to Deprescribing Cholinesterase Inhibitors: https://www.primaryhealthtas.com.au/ wp-content/uploads/2018/09/A-Guide-to-Deprescribing-Cholinesterase-Inhibitors-2019.pdf

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INHALERS

Inhalers DEPRESCRIBING GUIDANCE



Pulmonary Background

More than 8 out of 10 patients with obstructive lung disease in the U.S. experience inhaler device use-related errors.¹ In patients with end-stage pulmonary disease or advanced age, the risk of use-related errors is likely far greater.² Incorrect inhaler technique prevents patients from receiving optimal benefit from their inhalers. Many of the common step-by-step use errors are preventable by replacing the inhaler with nebulized therapy or an oral dosage formulation.¹ Nebulized medications tend to be a more efficient route of administration for patients with end-stage disease when compared to metered-dose or dry-powder inhalers. Switching inhaled corticosteroids to oral corticosteroids may provide palliation of additional symptoms including suppressed appetite, inflammatory pain, fatigue, and acute pulmonary exacerbations.³

Why Deprescribe?

RISKS ASSOCIATED WITH INHALER DEVICE CONTINUATION						
Lack of Benefit / Increased Risk	Improper inhaler technique may jeopardize adequate medication delivery resulting in poorer outcomes over time including greater risk of exacerbations, greater health resource utilization, and mortality. ¹					
Therapeutic Duplications / Polypharmacy	Lack of benefit from improper inhaler technique may lead to the prescribing of additional agents in an attempt to manage uncontrolled symptoms ⁴ resulting in increased overall medication exposure from duplicative therapies (e.g. long-acting bronchodilators + scheduled short-acting bronchodilators, inhaled corticosteroids + oral corticosteroids).					
Adverse Effects from Beta2-agonists* - anxiety, tachycardia, tremor Overexposure and/or Anticholinergics* - dry mouth, urinary retention Incorrect Use ⁵ Inhaled corticosteroids* - oral thrush, pharyngitis		Take Note: Adverse effect risk increases without additional clinical benefit with overuse and/or use of multiple agents in the same therapeutic class				

*See provided list of Common Inhaled Respiratory Medications for specific product examples within each therapeutic class.

Patient & Caregiver Talking Points

The BUILD Model provides a structured process to discuss deprescribing with patients, family, and caregivers.⁶ The basics of the BUILD mnemonic and sample conversational phrases for family and caregiver discussions are below.

BUILD	UNDERSTAND	INFORM	LISTEN	DEVELOP
A foundation of trust and respect	What the family knows about the device	The family about clinical evidence	To the family's goals and expectations	A plan of care in collaboration with family

Many patients are resistant to changing long-term medication regimens. Recognize that discussion on replacing inhalers may be interpreted by patients and families that the provider is "giving up", abandoning the patient, and might suggest that death is imminent. Use positive language and offer options; this shared decision-making approach may increase chances of successful deprescribing or conversion to more appropriate medication(s).

"Can you show me how you are using your inhalers? It's okay if you don't remember, we can review the steps together."

I "It seems you are having some difficulty using your inhalers. As your disease progresses it may be useful to make some adjustments to your medications. What worked before may not work as well for you now. Would you like to talk about making your medication routine a little less complicated?"

■ "There are other medications for shortness of breath/anxiety that may be more effective than your current inhalers."

"It sounds like it's hard for you to make a decision about stopping your inhaler. Can I share what my experiences and observations have been?"

"We really just want your breathing to be more comfortable. I want you to know this is a team effort and you're in charge of the team. I appreciate you allowing me to talk with you today."

"Before I visit next week, I'll give your doctor an update and get her input. She might suggest stopping the inhalers and using a nebulizer. Are you willing to give it a try?"

To the prescriber: "I have observed the patient who is unable to properly use the inhalers her anymore. I believe switching to a less complicated delivery system may greatly improve her outcomes. Are you okay with me making this change?"

How to Deprescribe

GOAL: Discontinue ineffective inhalers and reduce adverse effects while maintaining symptom control. Refer to the following approaches for pulmonary deprescribing guidance.

Most end-stage obstructive lung disease inhaler regimens can be consolidated to a nebulized short-acting beta2agonist / anticholinergic plus an oral corticosteroid (e.g., albuterol/ipratropium nebulized QID + prednisone by mouth QAM) supplemented with palliative measures for dyspnea management and various non-pharmacological techniques.

INHALER DEVICE WITH AN APPRO	PRESENT, CONSIDER DEPRESCRIBING OR REPLACING AN PRIATE MEDICATION(S) IN THE SAME THERAPEUTIC CLASS
Lack of Breathing Coordination	Inability to coordinate actuation of the inhaler device with a deep inhalation.
Lack of Inspiratory Capacity	Inability to deeply and forcibly inhale the medication to deliver it to the site of action deep into the lungs and hold breath for at least 5-10 seconds.
Lack of Physical Aptitude	Inability to actuate inhaler due to lack of dexterity and grip strength (e.g., severe arthritis in the hands).
Lack of Cognitive Aptitude	Patients with cognitive impairment (e.g., dementia) might not recall the proper step-by-step procedure for using an inhaler device.
Inhaler Inhalation Technique Errors Despite Continued Education	Review patient's ability to follow and perform device-specific step-by-step directions during all routine assessments (e.g., admission/recertification, decline in status, before ordering any refills, change in location).
Presence of Adverse Effects from Overexposure and/or Incorrect Use	Consolidate duplicative therapies in favor of less complicated delivery systems (see "Eliminate Therapeutic Duplications / Polypharmacy" algorithm).

ELIMINATE THERAPEUTIC DUPLICATIONS / POLYPHARMACY



ADDRESSING OTHER NON-STEROID ORAL PULMONARY MEDICATIONS

If the patient is also using any non-steroid oral pulmonary medications consider discontinuing if no longer clinically appropriate in end-of-life care or in advanced age (e.g. albuterol tabs, theophylline), or if a potential therapeutic duplication of therapy exists (e.g., montelukast or roflumilast with an oral corticosteroid).

CONSIDER OTHER DYSPNEA MANAGEMENT TECHNIQUES AS APPROPRIATE					
Non-Pharmacological Management	Minimize trigger risk, positioning sitting up, optimize environment by keeping room cool with lower humidity, increasing air movement with a fan, bedside relaxation techniques, provider psychosocial and spiritual support, smoking cessation, oxygen therapy ³				
Palliative Dyspnea Management ³	Short-acting opioids: low-dose morphine every 2 hours PRN for dyspnea				
	Benzodiazepines: low-dose lorazepam every 4 hours PRN for dyspnea- associated anxiety				
	Other nebulized agents for refractory dyspnea (e.g., normal saline, furosemide, fentanyl)				

COMMON INHALED RESPIRATORY MEDICATIONS⁵

Generic Name	Brand Name(s)	Dosage Form	Strength (Doses per Device)	Typical Dose
Short-Acting Beta2 Ago	onists (SABA) - Relax airw	ay smooth muscle (bronc	hodilation) by stimulating	beta2 receptors
Albuterol	Ventolin HFA, ProAir HFA, Proventil HFA, Accuneb	MDI Nebulizer	90 mcg per actuation (200)	MDI: 2 inh QID Neb: 3 mL via neb QID
Levalbuterol	Xopenex HFA, Xopenex	MDI Nebulizer	45 mcg per actuation (200)	MDI: 2 inh QID Neb: 3 mL via neb QID
Long-Acting Beta2 Ago	nists (LABA) - Relax airwa	ay smooth muscle (bronch	odilation) by stimulating	beta2 receptors
Indicaterol	Arcapta Neohaler	DPI	75 mcg per capsule (30)	1 cap inh Daily
Salmeterol	Serevent Diskus	DPI	50 mcg per blister (60)	1 inh BID
Olodaterol	Striverdi Respimat	MDI	2.5 mcg per actuation (28, 60)	2 inh Daily
Arfomoterol	Brovana	Nebulization	15 mcg per 2 mL	2 mL via neb BID
Formoterol	Perforomist	Nebulization	20 mcg per 2 mL	2 mL via neb BID
Short-Acting Muscarini in bronchial smooth mus	c Antagonists (SAMA) - P scle	rovide bronchodilation by	inhibiting acetylcholine at	: parasympathetic sites
lpratropium	Atrovent	MDI Nebulization	MDI: 17 mcg per spray (200) Neb: 0.5 mg per 2.5 mL	MDI: 2 inh QID Neb: 2.5 mL via neb QID
Long-Acting Muscarinic receptors	Antagonists (LAMA) - Pr	ovide bronchodilation by i	nhibiting acetylcholine at	type 3 muscarinic (M3)
Aclidinium	Turdoza Pressair	DPI	400 mcg per actuation (60)	1 inh BID
Tiotropium	Spiriva HandiHaler	DPI	18 mcg per capsule (30)	1 cap inh Daily
Tiotropium	Spiriva Respimat	MDI	1.25, 2.5 mcg per actuation (28, 60)	2 inh Daily
Umeclidinium	Incruse Ellipta	DPI	62.5 mcg per actuation (30)	1 inh Daily
Glycopyrrolate	Seebri Neohaler Lonhala Magnair	DPI Nebulization	DPI: 15.6 mcg per actuation (60) Neb: 25 mcg per 1 mL	DPI: 1 cap inh BID Neb: 25mcg via neb BID
Revefenacin	Yupleri	Nebulization	175 mcg per 3 mL	3 mL via neb Daily
Inhaled Corticosteroids migration and capillary	(ICSs) - Control inflammo permeability while increas	ation with slightly varying sing cellular lysosomal sta	mechanisms - most work Ibilization	by decreasing leukocyte
Beclomethasone	Qvar	MDI	40, 80 mcg per spray (120)	80 mcg inh BID
Budesonide	Pulmicort Flexhaler	DPI	90, 180 mcg per actuation (120)	180 mcg inh BID
Ciclesonide	Alvesco	MDI	80, 160 mcg per spray (60)	80 mcg 1 inh BID
Fluticasone	Flovent HFA	MDI	44, 110, 220 mcg per spray (120)	220 mcg 1 inh BID
	Flovent Diskus	DPI	50, 100, 250 mcg per actuation (60)	250 mcg inh BID

COMMON INHALED RESPIRATORY MEDICATIONS⁵

Generic Name	Brand Name(s)	Dosage Form	Strength (Doses per Device)	Typical Dose
Budesonide	Pulmicort Respules	Nebulization	0.25, 0.5, 1 mg per 2 mL	0.5 mg/2 mL via neb BID
Mometasone	Asmanex Twisthaler	DPI	110, 220 mcg per actuation (14, 30, 60, 120)	220 mcg inh BID

Combination Therapies - Combines two or more medications with different mechanisms of action (found above)					
SAMA/SABA Combinat	ions				
Ipratropium-Albuterol	Combivent Respimat DuoNeb	MDI Nebulization	MDI: 12/120 mcg per spray (120) Neb: 0.5 mg/2.5 mg per 3 mL	MDI: 1 inh QID Neb: 3 mL via nebulizer QID	
ICS/LABA Combination	S				
Budesonide- Formoterol	Symbicort	DPI	80/4.5, 160/4.5 mcg per actuation (120)	160/4.5 2 inh BID	
Fluticasone-Salmeterol	Advair HFA	MDI	45/21, 115/21, 230/21 mcg per spray (120)	115/21 2 inh BID	
	Advair Diskus	DPI	100/50, 250/50, 500/50 mcg per actuation (60)	250/50 1 inh BID	
Fluticasone-Vilanterol	Breo Ellipta	DPI	100/25 mcg per actuation (30)	1 inh Daily	
Mometasone- Formoterol	Dulera	MDI	100/5, 200/5 mcg per spray (120)	100/5 2 inh BID	
LAMA/LABA Combinati	ions				
Umeclidinium- Vilanterol	Anoro Ellipta	DPI	62.5/25 mcg per actuation (30)	1 inh Daily	
Tiotropium-Olodaterol	Stiolto Respimat	MDI	2.5/2.5 mcg per actuation (60)	2 inh Daily	
Glycopyrrolate- Formoterol	Bevespi Aerosphere	MDI	9/4.8 mcg per actuation (120)	2 inh BID	
Glycopyrrolate- Indacaterol	Utibron Neohaler	DPI	15.6/27.5 mcg per capsule (60)	1 cap inh BID	
ICS/LAMA/LABA Combinations					
Fluticasone- Umeclidinium- Vilanterol	Trelegy	DPI	100/62.5/25 mcg per actuation (14, 30)	1 inh Daily	

MDI: metered dose inhaler DPI: dry powder inhaler inh: inhalation

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TYPE 2 DIABETES MEDICATIONS

TYPE 2 DIABETES MEDICATONS DEPRESCRIBING GUIDANCE



Background

Type 2 diabetes (DM2) therapy traditionally focuses on intensive glycemic control, maintaining A1c < 6.5% or fasting glucose <130 mg/dL,¹ in order to lower the long-term risk of developing complications such as retinopathy, kidney disease, and neuropathy. At the end of life, tight glycemic control places patients at risk of hypoglycemia. Less intensive glycemic goals take into consideration limited life expectancy and reduce the risk of cognitive decline attributed to hypoglycemia.¹⁻⁵

Why Deprescribe?

In a national sample of Veterans Affairs nursing homes, 38% of hospice patients treated with insulin experienced hypoglycemia (glucose < 70 mg/dL), and 18% hospice patients experienced a severe episode (glucose < 50 mg/dL).⁵ Severe hyper- and hypoglycemia account for 2.6% of all hospitalizations and 2.5% of all 30-day readmissions according to a 2017 national cohort of adult patients with diabetes study.⁶ Additionally, an upward trend in emergency room visits for hypoglycemia from 2006 to 2011 saw the highest rates among adults aged 75 years or older.⁷ Engaging patients and families about managing diabetes at end-of-life helps guide expectations, maintain quality of life, and reduce reliance on emergent care.

Hospice patients with diabetes²⁻⁴

- Experience changes in their disease, medications, and diet that affect glucose levels
- Might not show signs of hyperglycemia but will experience symptoms of hypoglycemia
- May no longer want to inject insulin or monitor their glucose frequently enough to use insulin safely

Individualize the approach to blood glucose monitoring; do not test HbA1c and reduce frequency of fingerstick monitoring as much as feasible – e.g., three times per week if no longer taking insulin. If blood glucose testing is included in the care plan, use it to adjust therapy accordingly, not merely for documentation.^{8,9}

Patient & Caregiver Talking Points

The BUILD Model provides a structured process to discuss deprescribing with patients, family, and caregivers.¹⁰ The basics of the BUILD mnemonic and sample conversational phrases for family and caregiver discussions are below.

BUILD	UNDERSTAND	INFORM	LISTEN	DEVELOP
A foundation of trust and respect	What the family knows about the device	The family about clinical evidence	To the family's goals and expectations	A plan of care in collaboration with family

Educate patients and caregivers about how change in condition affects treatment and the risks of continuing tight glycemic control. Provide information on the signs and symptoms of both hyper- and hypoglycemia, especially when considering changes to diabetic medications and glucose testing. Patients may have only one sign or symptom, requiring vigilance from both the caregiver and clinician:

Hyperglycemia: Frequent urination, thirst, hunger, anxiety, confusion, irritability, headache, blurry vision, trouble concentrating, numbness, tingling, recurrent infections, impaired wound healing⁹

■ Hypoglycemia: Headache, confusion, dizziness, personality changes, fatigue, weakness, tiredness, sweating, shakiness, anxiety, elevated heart rate⁹

Many patients have a difficult time accepting that the monitoring and medication regimen can be liberalized after years of hearing about the importance of monitoring and strict glycemic control. Diabetes management can be an empowering and satisfying health promotion activity. This can be one of the last things many patients have to control as it relates to their health.

Recognize that discussion on loosening glycemic control may be interpreted by patients and families that the provider is "giving up" or abandoning the patient or might suggest that death is imminent. When indicated, and based upon patient's goals, recommend deprescribing antihyperglycemic oral medications and reducing the dose of insulin therapy to prevent hypoglycemia. Use positive language and offer options to the patient and family.^{4,11}

"We often find that people with diabetes and advanced illness might not benefit from their diabetic medication like they once did. I'm concerned that you are at risk for low blood sugars because of changes in your medications and diet. I'd like to review how to recognize and treat low blood sugar with you and your daughter."

"I'm worried that your mom's blood sugar is running low and her eating habits are irregular. Her appetite has really dropped off lately. Let's discuss changing some of her diabetes medications."

"It sounds like it's hard for you to consider stopping your dad's diabetes medications. Can I share what my experiences have been?"

"How do you feel about my recommendation to stop your Glucotrol®?"

How to Deprescribe

Avoiding hypoglycemia requires familiarity with the patient's daily oral intake, recognizing the hypoglycemic agents that commonly cause hypoglycemia and an understanding of the insulin's onset of action, peak (when insulin is at its highest glucose lowering effect) and duration of effect.

TABLE 1 - DIABETES MEDICATION				
Class	Generic	Hypoglycemia common? ¹²⁻¹⁴		
Sulfonylureas	Glipizide (Glucotrol®) Glimepiride (Amaryl®) Glyburide (DiaBeta®)	Chlorpropamide (Diabinese®) Tolazamide (Tolinase®) Tolbutamide (Orinase®)	Yes (highest)	
Meglitinides	Nateglinide (Starlix®)	Repaglinide (Prandin®)	Yes (low risk)	
Biguanide*	Metformin (Glucophage®)		No	
Sodium-glucose linked	Empagliflozin (Jardiance®)	Dapagliflozin (Farxiga®)	No	
inhibitors*	Canagliflozin (Invokana®)	Ertugliflozin (Steglatro®)		
Thiazolidinediones (TZDs)	Pioglitazone (Actos®)	Rosiglitazone (Avandia®)	No	
Dipeptidyl peptidase-4 (DPP-4) inhibitors*	Alogliptin (Nesina®) Linagliptin (Tradjenta®)	Saxagliptin (Onglyza®) Sitagliptin (Januvia®)	No	

Class	Generic	Hypoglycemia common? ¹²⁻¹⁴	
Glucagon-like, peptide-1 (GLP-1) agonists or incretin mimetic	Dulaglutide (Trulicity®) Exenatide (Byetta®) Exenatide ER (Bydureon®) Liraglutide (Victoza®) Lixisenatide (Adlyxin®)	Semaglutide (Ozempic®, Rybelsus®) Liraglutide-insulin degludec (Xultophy®) Lixisenatide-insulin glargine (Soliqua®)	No, monotherapy Yes, with insulin
Alpha-glucosidase inhibitors	Acarbose (Precose®)	Miglitol (Glyset®)	No

*medications in this class are also available as combination products, increasing risk for hypoglycemia and therapeutic duplication

Insulin Type	Products	Appropriate Candidates for Continued Insulin Use 8,12-14
Rapid-acting	Humalog®, Ademlog® (insulin lispro) NovoLog®, Fiasp® (insulin aspart) Apidra® (insulin glulisine)	For patients with sporadic eating habits or those that miss meals due to nausea and/or vomiting or anorexia willing and capable to administer frequent injections independently or with support in home.
Short-acting (Regular)	Human insulin (rDNA origin) (Humulin® R, Novolin® R)	For patients with variable oral intake (or in whom oral intake is diminishing) and willing and capable to administer frequent injections independently or with support in home.
Intermediate-acting (NPH)	Human (rDNA) isophane (Humulin® N, Novolin® N)	For patients with a history of glucose control on rapid-acting or short-acting insulins willing and capable to administer 2 injections per day independently or with support in home. Oral intake should be stable.
Long-acting	Lantus® (insulin glargine) Levemir® (insulin detemir) Toujeo® (insulin glargine)	Long-acting insulin may cause less hypoglycemia as they have no significant peak effect. For patients with a history of glucose control on rapid-, short- or intermediate-acting insulins willing and capable to administer 1 injection per day independently or with support in home. Oral intake should be stable.
Ultra long-acting	Tresiba® (insulin degludec)	Place in therapy for hospice patients has not been established.
Insulin mixtures	NovoLog Mix® 70/30 Humalog Mix® 75/25 & 50/50 Humulin® & Novolin® 70/30	Initiated in treatment-naïve patients. Patients on hospice may be maintained on these therapies while stable, however, it is a rare to convert other insulin therapies into an insulin mixture regimen.

Reasonable Treatment Goals in Hospice

- Avoid hypoglycemia while minimizing symptoms of sustained hyperglycemia syndromes
 - Hyperosmolar hyperglycemic state (HHS) with blood glucose >750 mg/dL
 - Diabetic ketoacidosis (DKA) with blood glucose levels >300 mg/dL (rare for DM2)
- Simplification of complex regimens
 - Discontinue non-insulin hypoglycemic agents
- Minimize the burdens of diabetes treatment (e.g., stop A1c testing, decrease frequency of blood glucose checks and finger sticks, discontinue sliding scale insulin)⁹

When limited remaining life expectancy makes benefit uncertain, a reasonable A1c goal is <8.5% (average blood glucose of about 200 mg/dL).¹

Blood Glucose Targets

Advanced disease and relatively stable - several months to a year life expectancy

- No changes at this point unless requested by patient or family; dosing reflects goal of avoiding hypoglycemia, less intensive monitoring, and tailored to oral intake
- Regimen tailored to target fasting glucose <200 mg/dL8,¹⁵

Impending death (e.g., organ failure or limited oral intake) - several weeks or less life expectancy

- Adjust medication regimens to avoid hypoglycemia
- Recommend decreasing or stopping insulin and sulfonylurea medications
- If continuing insulin, liberalize therapy to maintain fasting glucose around 200 mg/dL8,¹⁵

Actively dying (e.g., multiple organ system failure, end of life symptoms such as agonal respirations) – life expectancy is usually hours to days: Goal is patient comfort; glycemic control is not a priority.

- Type 1 diabetes: Liberal target (e.g., <360 mg/dL) and insulin continued only if patient is prone to DKA
- Type 2 diabetes: Discontinue all oral and injectable diabetes medications and insulin^{8,15}

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Additional Resources

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Statins DEPRESCRIBING GUIDANCE



Background

Statins are the most effective and best tolerated medications for treating dyslipidemias.^{1,2} Through systematic evidence review, statins have shown reduced cardiovascular (CV) events when used for both primary (reducing the chance of disease before it happens) and secondary prevention (slowing down the progression of illness).¹ The benefit that statins can provide to patients is clear, especially with recent guidelines that greatly expand the population of patients who may qualify for statin therapy.¹ Hyperlipidemia does not present with symptom management that would need palliation and evidence suggests that survival is not affected;² hyperlipidemia does not contribute to the patient's 6 month or less prognosis.³ Even the most recognized proponent of statins for cholesterol management, the American College of Cardiology/American Heart Association Task Force, recognizes the need for shared decision-making including discussions on deprescribing statins in older adults with multimorbidity, frailty, fall risk, sarcopenia, and cognitive decline.¹

	TABLE 1 - STATINS	
Atorvastatin (Lipitor®)	Lovastatin (Altoprev®)	Rosuvastatin (Crestor®, Ezallor® Sprinkle)
Simvastatin (FloLipid®, Zocor®)	Fluvastatin (Lescol XL®)	Pravastatin (Pravachol®)
	Pitavastatin (Livalo®, Zypitamag®)	

Why Deprescribe?

Optimize drug therapy to be consistent with the patient's treatment goals

Statins are preventative therapy and do not facilitate comfort or enhance quality of life.² Discontinue statins if the patient does not wish to pursue preventative therapies.

- At end of life, benefits of lipid-lowering medication are unlikely to outweigh risk; consider cardiovascular events, performance status and quality of life, fatigue, impact on memory, and muscle-related pain symptoms.²
- Reduce the burden of pharmacotherapy by discontinuing non-palliative medications.
- Improve quality of life by reducing risk of muscle problems such as aches, pains, and/or weakness. Deprescribing statins may also reduce falls, lessen memory loss, and decrease nausea, constipation, and diarrhea.²
- A recent randomized clinical trial has shown that discontinuing statin therapy may have positive benefits for patients while not increasing risk of death. Among the outcomes, quality of life scores were higher and there were no differences in median time to death or time to first CV event between study groups.⁴

Align medication use with the patient's prognosis and continued benefit of drug therapy

The purpose of taking a statin is to reduce the occurrence of major CV events in high risk patients. Compared to non-users, significant reduction of CV events does not happen until 2 or more years of therapy.^{2,3} Time to benefit in primary prevention of fatal and non-fatal MI ranges from 1.9 to 5.3 years for statins.⁴

- For primary prevention, the time to benefit is estimated at over 2 years.^{2,3}
- For secondary prevention, some evidence shows potential benefit at 16 weeks with high-intensity doses.^{2,3}

- Newly initiated statin therapy after acute stoke or TIA shows significant risk reduction after 5 years.⁵
- In a meta-analysis of primary prevention trials, researchers concluded that in elderly subjects at high CV risk without established CV disease statins do not significantly prolong survival.⁶
- Statin therapy does not appear to show benefit within a 6-month prognosis window and are considered unnecessary medications for hospice patients.²

Minimize side effects and maximize safety of the medication regimen by determining if the patient is at risk of harm by continuing therapy

- Elderly patients and those near end of life experience declining organ function and altered metabolism which may explain the lack of benefit and increased risk of side effects with statin therapy (Table 2).¹⁻⁵ Prescribe statins caution in patients over 65 and those with renal or hepatic impairment due to increased risk of myopathy.⁷ If a patient complains of severe muscle symptoms or fatigue, discontinue the statin immediately.
- Loss of swallowing ability should prompt medication review and discussion of deprescribing.
- Statins, with the exception of pravastatin, are highly protein bound. Patients with malnutrition or decreased serum protein levels, are more likely to experience muscle pain as a result of statin toxicity.¹

TABLE 2 – COMMON SIDE EFFECTS OF STATIN THERAPY					
headache	nausea	arthralgia	extremity pain	myopathy	
diarrhea	insomnia	upper respiratory tract Infection	musculoskeletal pain	fatigue	
dyspepsia	cognitive impairment	urinary tract Infection	myalgia	arrhythmia	
cough	dizziness/vertigo	chest pain	constipation	abdominal pain	

Consider additional potential harms

- Lipid lowering agents are considered preventative medication and do not provide comfort or symptom relief.²
- Ongoing lab monitoring is recommended to guide statin therapy: regular lipid panels and periodic liver function testing^{1,7}
- Some studies show a potential risk of exacerbating diabetes. Statins can impair insulin release by inhibiting insulin secretion, effecting glucose metabolism.^{8,9}
- Patients with underlying liver or renal impairment are at an increased risk for hepatotoxicity, myopathy, rhabdomyolysis, and hematuria, especially with higher-dose statins (e.g., rosuvastatin 40mg, simvastatin 80mg, atorvastatin 80mg)⁷

Reduce the potential for drug interactions between statins and medications that are commonly prescribed at end of life:⁷

- Macrolide antibiotics (e.g., azithromycin, clarithromycin, erythromycin) and azole antifungals (e.g., itraconazole, fluconazole, ketoconazole) may increase serum statin levels leading to adverse events rhabdomyolysis, acute renal failure.⁷
- Some anticoagulants [e.g., warfarin, dabigatran (Pradaxa®), ticagrelor (Brilinta®)] may increase serum statin levels leading to increased risk for statin toxicity or increased risk of bleeding.⁷
- Grapefruit juice consumption may increase serum statin levels, particularly with simvastatin. Patients taking simvastatin should avoid grapefruit juice.

Patient & Caregiver Talking Points

The BUILD Model provides a structured process to discuss deprescribing with patients, family, and caregivers.¹⁰ The basics of the BUILD mnemonic and sample conversational phrases for family and caregiver discussions are below.

BUILD	UNDERSTAND	INFORM	LISTEN	DEVELOP
A foundation of trust and respect	What the family knows about the device	The family about clinical evidence	To the family's goals and expectations	A plan of care in collaboration with family

Patients are often concerned about stopping medications they may have been taking for a long time to prevent or slow disease progression. The deprescribing process is driven by available clinical evidence and clinician experience caring for patients at end of life. Discontinuing statins does not affect patient prognosis or survival but provides benefit by reducing risk of drug interactions, adverse events, and problematic side effects.

All deprescribing decisions are made in collaboration with the hospice interdisciplinary team and the patient's attending physician or other health care providers.

Hospice and palliative care clinicians recommend deprescribing statins for patients in declining health, with renal or liver impairment, and if the expected prognosis is less than 6 months.

- > "We understand this can be stressful and you may have fears, worries or feel guilty stopping these medications. If you're not ready right now, let's plan to talk about it again later."
- > "What did your doctor tell you about the Crestor? What are your goals for this medication? The hospice team will continue to visit every week or so and your hospice nurse will keep track of your vitals. If we see any concerns, we will get in touch with your cardiologist."
- > "Our goal is to provide comfort, but your mom's simvastatin seems to be making her leg pain worse. Before we increase her pain medication dose again, let's try discontinuing this statin. Did you know statins can cause muscle pain in older adults, especially when their kidneys aren't as healthy as they used to be?"
- > "Your father seems to be declining and is having some difficulty swallowing. Have you noticed this? Wouldn't it be easier for him, and for you, if you didn't have to crush so many medications into applesauce? He might eat a bit more regular food that way too."

How to Deprescribe

- Statins may be discontinued without tapering. In hospice care, the risk of continuing statins exceeds any potential benefit.²
- Candidates for deprescribing statins include patients with reduced or limited life expectancy, those with a low risk of cardiovascular events, or patients experiencing side effects of statins such as muscle pain and fatigue.²

References & Additional Resources

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Disclaimer

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