Deprescribing Guide: Diabetes Medications

INTRODUCTION TO DIABETES MEDICATION DEPRESCRIBING

The pharmacologic management of Type 2 diabetes focuses on intensive blood glucose control, with intent to maintain an A1c of <6.5% or fasting glucose level to < 130mg/dl. These glucose goals are set to lower the long-term risk of developing the most commonly experienced side effects of hyperglycemia, which include neuropathy, kidney disease, retinopathy, and cardiovascular disease. However, in the setting of a life-limiting illness, the goals of glycemic management change from preventing the effects of hyperglycemia to avoiding the dangers of hypoglycemia. Thus, the A1c target relaxes to closer to 8 and blood glucose levels 200mg/dL or even higher if patient remains asymptomatic. Considering this paradigm shift, several classes of diabetes medications do not directly contribute to improved glycemic management or symptom management and may cost > $600/month. At the end of life, less intensive management of blood glucose goals reduce the risk of cognitive decline attributed to hypoglycemia.

COMMON DIABETES MEDICATIONS

Medication Class	Medication Name		Hypoglycemia	Cost
Sulfonylureas	Glipizide (Glucotrol®) Glimepiride (Amaryl®) Glyburide (DiaBeta®)	Chlorpropamide (Diabinese®) Tolazamide (Tolinase®) Tolbutamide (Orinase®)	High Risk	$
Meglitinides	Nateglinide (Starlix®)	Repaglinide (Prandin®)	Low Risk	$$
Biguanide	Metformin (Glucophage®)		No Risk	$
SGLT-2 Inhibitors	Empagliflozin (Jardiance®) Canagliflozin (Invokana®)	Dapagliflozin (Farxiga®) Ertugliflozin (Streglatro®)	No Risk	$$$
Thiazolidinediones	Pioglitazone (Actos®)	Rosiglitazone (Avandia®)	No	$$$
DPP-4 Inhibitors	Alogliptan (Nesina®) Linagliptan (Tradjenta®)	Saxagliptan (Onglyza®) Sitagliptan (Januvia®)	No	$$$
GLP-1 Agonists	Dulaglutide (Trulicity®) Exenatide (Byetta®) Liraglutide (Victoza®)	Semaglutide(Ozempic®) Lixisenatide (Adlyxin®)	No	$$$
Alpha-Glucosidase Inhibitors	Acarbose (Precose®)	Miglitol (Glyset®)	No	$$$

Insulin Type	Available Products	Candidates for continued use
Rapid-acting	Insulin lispro (Humalog®, Admelog®) Insulin aspart (NovoLog®, Fiasp®) Insulin glulisine (Apidra®)	Patients with sporadic eating habits, missing meals due to n/v or anorexia **AND** able to administer independently
Short-acting (Regular)	Human Insulin (Humulin R®, Novolin R®)	Patients with variable intake **and** willing to give frequent injections
Intermediate (NPH)	Human isophane (Humulin N®, Novolin N®)	Stable oral intake, history of glucose control on rapid or shrort acting insulin
Long-acting	Glargine (Lantus®, Toujeo) Levemir (Detemir)	Likely to cause less hypoglycemia due to lack of peak effect
Ultra-long acting	Insulin degludec (Tresiba®)	Place in therapy not established (hospice)
Mixed Insulins	Insulin 70/30	Rare to continue or convert to on hospice

The decision to discontinue diabetes 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.

RATIONALE FOR DEPRESCRIBING

Recent a recent study following hospice patients prescribed insulin, 38% experienced hypoglycemia (glucose <70mg/dL), and 18% experienced a severe episode (glucose < 50mg/dL). Additionally, an upward trend in emergency room visits for hypoglycemia saw the highest rates among adults 75 years of age and older. It is critical to have discussions with the patient and caregivers about the management of blood glucose while on hospice to prevent undesired outcomes that could negatively impact quality of life and reduce reliance on emergent care.

When considering how to most appropriately manage diabetes in a patient on hospice, it is important to consider the following:

Consider deprescribing for any of the following reasons:	
Symptomatic hypoglycemia	• Often when diagnosed with a life limiting illness, patients experience changes in their disease, active medication profile, and nutrition/intake • These changes often result in decreased blood glucose levels • Continued use of diabetes medications may significantly increase the risk of a hypoglycemic event • Hypoglycemia is much more likely to result in symptomatic episode, possibly even requiring emergent care to resolve

No longer indicated	• No symptom management benefit provided by most diabetes medications • SGLT-2 and DPP-4 inhibitors as well as GLP-1 agonists are often used for long-term mortality benefits, not acute mgmt. • Agents from these classes are often very expensive
Goals of care	• Patient may no longer desire to experience syringe injections or lancet pinpricks • Once enrolled in hospice, the goal of diabetes management transitions to avoiding the symptomatic ends of the glucose spectrum

PATIENT & CAREGIVER DISCUSSION POINTS:

- 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 or modify diabetes 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, such as the following from the National Hospice and Palliative Care Organization deprescribing guidelines:
    - "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

1.	Initially, recommend educating patients and caregivers about that their changing condition and how tight glycemic control can increase risk of hypoglycemia. Then recommend sharing the common side effects of each condition, which include: ○ Hyperglycemia: Frequent urination, thirst, hunger, anxiety, confusion, irritability, headache, blurry vision, trouble concentrating, numbness, tingling, recurrent infections, impaired wound ○ Hypoglycemia: Headache, confusion, dizziness, personality changes, fatigue, weakness, tiredness, sweating, shakiness, anxiety, elevated heart rate
2.	Recommend individualizing 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
3.	If family or patient is hesitant to discontinue, consider a trial discontinuation for a limited period (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.
4.	When determining which agents to stop first, remember that patients on hospice have a limited life expectancy of 6 months or less, therefore SGLT-2 and DPP-4 inhibitors as well as GLP-1 agonists not of benefit to continued.
5.	Consider discontinuation of rapid-acting insulin for patients with limited intake due to concern of hypoglycemia. May also consider dose reduction/decreasing dose of long-acting insulin in patient with diabetes who has significant decrease in nutritional intake. Can always monitor for symptoms of hyperglycemia and re-initiate therapy if necessary
6.	Re-evaluate. Due to the ever-changing nature circumstances of patients on hospice, review medication regimens for deprescribing opportunities more than just upon admission.

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