PHARMACIST'S LETTER

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PRESCRIBER'S LETTER

Drugs That Significantly Increase Blood Glucose

Clinicians may be surprised by the number of drugs that can cause an increase in blood glucose. In certain patient populations, such as those with glucose intolerance, this may be more likely to be of significance. It may also be of more significance for drugs that are used chronically, such as antipsychotics or statins. In some cases an alternate medication or formulation can be used, such as with niacin. In other cases, such as with statins, the benefits of using the drug may outweigh any potential risks. In any case, it is generally advised to monitor blood glucose more closely when patients with impaired glucose tolerance start a drug that can increase blood glucose. The following chart lists commonly used medications that can cause an increase in blood glucose and risk of diabetes, and tips for management.

Drug or Drug Class	Potential Mechanisms	Increased Risk of Diabetes?	Reversible When Drug is Stopped?	Considerations for Management
Atypical Antipsychotics	•Weight gain, reduced insulin sensitivity[1,2] •Risk may be highest with clozapine and olanzapine and lowest with aripiprazole and ziprasidone[1]	Yes[1]	In some cases[1]	•Monitor BMI and waist circumference at baseline, then every 4 weeks for the first 3 months of therapy, then once every 3 months[1] •Monitor fasting blood sugar at baseline, 12 weeks, and then at least annually[1] •Switch to a lower risk agent if possible in patients with drug-induced diabetes[1]
Beta-Blockers	•Reduced insulin secretion and sensitivity[1,2] •Effects on blood sugar may be less likely with nonselective beta-/alpha-blockers (e.g., carvedilol)[1-4]	Data are conflicting[2,5]	Yes[3] (Effects on blood sugar may be transient and of little clinical significance)[3]	•Counsel patients about symptoms of hyperglycemia

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Drug or Drug Class	Potential Mechanisms	Increased Risk of Diabetes?	Reversible When Drug is Stopped?	Considerations for Management
Corticosteroids	•Increased hepatic gluconeogenesis, reduced insulin sensitivity[2,6-8] •Typical onset is within 8 weeks of starting therapy, but can occur as soon as the first day of therapy.[6,22] •Risk is increased with oral route, higher doses (including topical/inhaled steroids), longer durations of therapy, and use in patients with glucose intolerance[2,7,22]	Yes[2,7] (Replacement doses do not appear to increase the risk of diabetes)[2]	In some cases[6,7] (May also resolve during therapy)[6]	•Monitor blood sugar. Some experts recommend monitoring daily during the first 2 to 3 days of treatment for patients who start medium to high doses of oral steroids and for patients with diabetes or risk factors for diabetes who start low doses of oral steroids.[7] Others recommend checking 1 week after starting treatment.[8] •Counsel patients about symptoms of hyperglycemia[8] •Insulin is generally the preferred treatment for corticosteroid-induced hyperglycemia[7,8]
Diuretics Thiazides Loops	•Impaired insulin secretion (secondary to hypokalemia), reduced insulin sensitivity[2,4,9] •Loop diuretics are less likely to cause metabolic side effects than thiazides[3,9] •Low blood levels of magnesium or potassium are associated with increased risk of hyperglycemia with thiazides[2,3,9]	Yes[5,9,10]	Yes[4,11]	•Counsel patients about symptoms of hyperglycemia •Limit doses of hydrochlorothiazide to 25 mg daily and chlorthalidone to 12.5 mg daily to help reduce the risk of metabolic side effects[3] •Maintain blood levels of potassium between 4 and 5 mEq (mmol)/L[3,4]
HIV meds Protease inhibitors (PI) Nucleoside reverse transcriptase inhibitors (NRTI)	•For PIs, peripheral insulin resistance, impaired glucose tolerance[4] •Atazanavir may be less likely to cause hyperglycemia than other PIs[4] •Pancreatic toxicity with NRTI[4] •Typical onset is about 60 days after starting therapy[12]	Yes[4]	Yes[4]	•Counsel patients about symptoms of hyperglycemia[4] •Monitor blood sugar at initiation of therapy, 3 to 6 months later, and then annually[12]

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Drug or Drug Class	Potential Mechanisms	Increased Risk of Diabetes?	Reversible When Drug is Stopped?	Considerations for Management
Immunosuppressants Cyclosporine Tacrolimus	•Pancreatic beta-cell toxicity, reduced insulin release, and reduced insulin sensitivity[2,4]	Yes[4]	In some cases[4]	•Counsel patients about symptoms of hyperglycemia
Niacin	•Insulin resistance, increased hepatic gluconeogenesis[2,13] •Blood glucose increases in nondiabetic patients are small, but may be clinically significant in patients with diabetes.[13] The risk for hyperglycemia is increased with higher doses of niacin.[14] •Long-acting dosage forms may be less likely to cause hyperglycemia[2]	Yes[2]	Yes[2] (May also resolve during therapy)[13]	•Counsel patients about symptoms of hyperglycemia •Monitor blood sugar in patients with diabetes who start niacin, adjust diabetes meds if necessary[14] •Discontinue niacin in patients with uncontrolled hyperglycemia[2]
Quinolones	•Mechanism is unclear[15] •Usually presents after several days of therapy[15] •Risk of hypoglycemia or hyperglycemia appears to be greater with levofloxacin than with ciprofloxacin.[16] Risk may be highest with moxifloxacin.[17] •Patients with diabetes, on high doses of quinolones with reduced renal function, concomitant corticosteroid use, and older age may be at higher risk of blood glucose abnormalities[15]	Has not been shown	Yes	•Adhere to recommend doses[15] •Counsel patients taking quinolones about the signs of both hypoglycemia and hyperglycemia[15]

Drug or Drug Class	Potential Mechanisms	Increased Risk of Diabetes?	Reversible When Drug is Stopped?	Considerations for Management
Statins	•There are a number of proposed mechanisms, including muscle insulin resistance. More than one mechanism may contribute.[18,19] •The risk of new onset diabetes may be higher with higher potency statins (e.g., rosuvastatin) and with higher doses of statins[10,18] •Risk may be limited to individuals with risk factors for diabetes.[14] Women, the elderly, and Asians may also be at higher risk.[20]	Yes[10] (slight increased risk)	Discontinuing statins is not generally recommended since cardiovascular benefits outweigh the risk of new onset diabetes[14,21]	•Consider the potential benefit of diabetes screening in patients at risk[10,14,20]

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