Medications Cheat Sheet

This cheat sheet offers an easy to remember guide to what medication is "not likely" to be used in certain situations. Note that "not likely" is **NOT** the same as "for certain". You must use your clinical judgement with each question and patient in real life. For example, a patient does not want to gain weight but is dying from acute diabetic ketoacidosis. What do you recommend? A) metformin B) acarbose C) sitagliptin D) insulin. The answer would be insulin even though the patient does not want to gain weight. Use your clinical judgement, read the question fully and remember that "not likely" is **NOT** the same as "for certain". Note that the mechanism of action (MOA) for some of the side effects are unknown and I will give the most popular explanation, but the exact explanation is unknown.

Patient scenario	Use Not Likely	Because:
Patient wants to lose weight or is obese	Insulin Thiazolidinediones i.e., Avandia (rosiglitazone) Actos (pioglitazone) Sulfonylureas i.e., Diamicron (gliclazide) Diabeta (glyburide) Meglitinides i.e Gluconorm (repaglinide)	Weight gain can be a touchy subject for patients. It can be discouraging to be told to lose weight to help your diabetes, but then we are going to give you a medication that makes you gain weight. Its important to discuss the benefits of a lower A1c and to listen to your patient's concerns. The 5A's from Obesity Canada are useful tools. Insulin is an anabolic hormone that stimulates storage of glucose into the cells which leads to weight gain. Thiazolidinediones promote weight gain by increasing insulin sensitivity and fluid retention. Sulfonylureas and meglitinides increase insulin secretion
Bladder Cancer	Actos (pioglitazone) Forxiga (dapagliflozin) *For the exam yes, but in real life, no*	Meta analyses of pioglitazone have shown slight increases in rates of bladder cancer. In preliminary research, pioglitazone was shown to increase bladder cancer in rats. Dapagliflozin, when it first came out, had a contra-indication with bladder cancer. However further research has shown no association, and the contraindication has been removed from the product monograph in Aug/21. Surprisingly, the warning has not been removed from the guidelines yet. Go with guidelines for the exam.
Wants to avoid hypoglycemia	Insulin Sulfonylureas Meglitinides	These medications have the highest chance of causing hypoglycemia relative to other oral diabetes medications. Their use should be avoided if the pt is at high risk of falls, has a job that operates heavy machinery, etc. It doesn't mean you can't use them, but you need to adjust the dose carefully. Also review the causes, treatment and ways to prevent hypoglycemia thoroughly with patients.
Heart Failure	Thiazolidinediones Onglyza (saxagliptin)	Actos (pioglitazone) and Avandia (rosiglitazone) can both cause fluid retention which can worsen heart failure. Studies of Onglyza (saxagliptin) showed increased hospital-ization for heart failure as compared to the placebo group

Very low blood pressure	SGLT-2 inhibitors i.e Invokana (canagliflozin) Forxiga (dapagliflozin) Jardiance (empagliflozin	SGLT-2 inhibitors increase urination and have effects similar to thiazide diuretic like hydrochlorothiazide or indapamide. This can lead to a 4–10 mmHg reduction of systolic blood pressure. If your pt's BP is high than this is a beneficial side effect. However, if your pt's BP is low the addition of an SLGT-2 I may push them into hypotension.
Thyroid Cancer or Multiple endocrine neoplasia (MEN) syndrome (type 2)	GLP-1 analogs i.e., Victoza (liraglutide) Trulicity (dulaglutide) Ozempic (subcutaneous semaglutide) Rybelsus (oral semaglutide) Mounjaro (tirzepatide)	There are 4 main types of thyroid cancer: medullary, papillary, follicular, and anaplastic. GLP -1 analogs, in rat studies, increased the risk of medullary thyroid cancer. Therefore GLP-1 analogs are contraindicated in pt's with a family or personal history of medullary thyroid cancer. Multiple endocrine neoplasia (MEN) syndromes are rare inherited disorders (different types) in which several endocrine glands develop tumors or grow excessively without forming tumors. Since GLP-1 analogs, in rat studies, increased the risk of thyroid cancers they are contraindicated in pt's with MEN syndrome (type 2)
Frequent yeast infections or urinary tract infections	SGLT-2 inhibitors i.e Invokana (canagliflozin) Forxiga (dapagliflozin) Jardiance (empagliflozin)	SGLT-2 inhibitors block the absorption of glucose in the kidneys. This increases the amount of glucose in the urine. The more glucose in the urine the more conducive the genital area is to bacterial and yeast infections.
On Plavix (clopidogrel) or Lopid (gemfibrozil)	Gluconorm (repaglinide)	There is a drug interaction with clopidogrel and repaglinide which increases the concentration of repaglinide 4-5x times leading to hypoglycemia. A similar interaction happens with gemfibrozil increasing repaglinide concentration by 8x times leading to hypoglycemia.
Bone issues	Actos (pioglitazone) Invokana (canagliflozin)	Several studies have shown that pioglitazone increases bone fracture risk especially in the distal bones of the arms and legs. Pioglitazone activates the PPAR system which improves insulin sensitivity. One of the popular theoretical explanations is that some isoforms of PPAR are expressed in osteoclasts. When activated it causes increased bone breakdown. Canagliflozin can increase the risk of fractures as well. One of the popular theoretical explanations is that it affects calcium and phosphate levels in the blood. Caution should be used for both drugs if the patient has osteoporosis or other fracture risks. Other SLGT-2 inhibitors and thiazolidinediones do not seem to increase fracture risk.
On a limited income with no drug coverage	GLP-1 analogs SGLT-2 inhibitors DPP-4 inhibitors	For people on a fixed or limited income these medications may be too expensive to afford. This is a important barrier to review in real life and in the exam.

Pre-existing Retinopathy	GLP-1 analogs (insulin)	The most popular explanation for this side effect is that significant drops in A1c can precipitate a transient worsening in retinopathy. This s/e is also seen with insulin in other studies.
Sensitive Stomach/Severe gastrointestinal (GI) Issues/ Does not want GI issues	Biguanides i.e. Glucophage (metformin) GLP-1 Analogs Alpha-glucosidase inhibitor I.e. Glucobay (acarbose) Gastrointestinal Lipase Inhibitor I.e. Xenical (Orlistat)	This is one that requires a lot of interpretation. The listed medications usually cause GI upset. If the patient lists GI upset as a major concern, then the medication may not be a good choice. However, I do have patients with sensitive stomachs who tolerate low doses of metformin and GLP analogs just fine.
Sucrose cannot be used to treat hypoglycemia	Acarbose	Acarbose inhibits the breakdown of sucrose into fructose and glucose. If a patient is experiencing hypoglycemia, then giving sucrose wont help. You will need to use dextrose or honey, or if both are unavailable, milk, as lactose breakdown is not inhibited by acarbose.
Gallstone disease	GLP-1 analogs	Rarely, GLP-1 analogs can cause gallbladder contraction leading to gallstones. DPP-4 inhibitors do not affect incretins strongly enough to affect gallbladders.
Concerned about CV safety	Avandia (rosiglitazone) Glyburide (gliclazide preferred)	The DREAM study seemed to show a trend toward CV harm with rosiglitazone and was stopped early. Another metanalysis done at that time also raised concerns of increased risk of MI and CV death. Since then, there have been conflicting research showing none or some increased risk. Regardless rosiglitazone is almost never used anymore as there are better options. Pioglitazone does not seem to increase CV risk. Some research (though conflicting) has shown that sulfonylureas may increase CV risk (possibly through hypoglycemia). Gliclazide is preferred over glyburide due to lower risk of CV events and mortality.
Pancreatitis and/or pancreatic cancer	DPP-4 inhibitors for pancreatitis and/or pancreatic cancer GLP-1 analogs for pancreatitis only, no pancreatic cancer	One popular explanation is that Incretins can cause proliferation of the cells in the pancreas. If the incretins cause too much replication than the cells distort the micro-ducts and there is obstructed outflow leading to inflammation and pancreatitis which may result in pancreatic cancer. DPP-4 inhibitors and GLP-1 analogs should be used with caution in these cases.
Vitamin B12 deficiency	Biguanides	Metformin seems to interfere with the intrinsic factor needed for vitamin B12 absorption in the terminal ileum of the GI tract.

Pre-existing Retinopathy	GLP-1 analogs (insulin)	The most popular explanation for this side effect is that significant drops in A1c causes a transient worsening in retinopathy. This s/e is also seen with insulin. See SUSTAIN 6 for details. Can still use GLP-1 but cautiously.
Risk of Diabetic ketoacidosis (DKA) and low carbohydrate diets	SGLT-2 inhibitors	SGLT-2 inhibitors increase the risk of DKA. There are multiple theories on why this occurs but nothing concrete. SLGT-2 inhibitors should be used in caution in people who have had previous episodes of DKA. Adhering to a low carbohydrate diet increases ketosis which may increase the risk of DKA. Adding a SLGT-2 inhibitor would add further risk.
Loss of protective sensation, prior foot ulcers or lower limb amputations	SGLT-2 inhibitors	In the canagliflozin study, CANVAS, there was an increased incidence of foot/toe amputations. This effect was not found in other SGLT-2 studies. More recent studies have shown that canagliflozin does not seem to have this side effect. However, the canagliflozin monograph still has a black box warning on lower limb amputations so it should not be used together. For the other SGLT-2 inhibitors good foot care is recommended.
Unable to hold down fluids or is dehydrated	S- Sulfonylureas and meglitinides A- ACE inhibitors D- Diuretics, direct renin inhibitors M-Metformin A- Angiotensin Receptor Blockers N- Non-steroidal anti-inflammatory S-SGLT-2 inhibitors	Memorize SADMANS for the exam. Please see Appendix 8 of the 2018 Clinical Practice guidelines on page S316 for more details. Dehydration can cause a reduction in renal function leading to: S- a decrease in the renal clearance of sulfonylureas and meglitinides leading to accumulation and possible hypo (see updated SADMANS in After Exam Review) A- may reduce renal function further D- may further dehydrate patient M- a decrease in the renal clearance of metformin leading to increased levels and possible lactic acidosis A- may reduce renal function further N- may reduce renal function further S- may further dehydrate patient and increase the risk of diabetic ketoacidosis

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