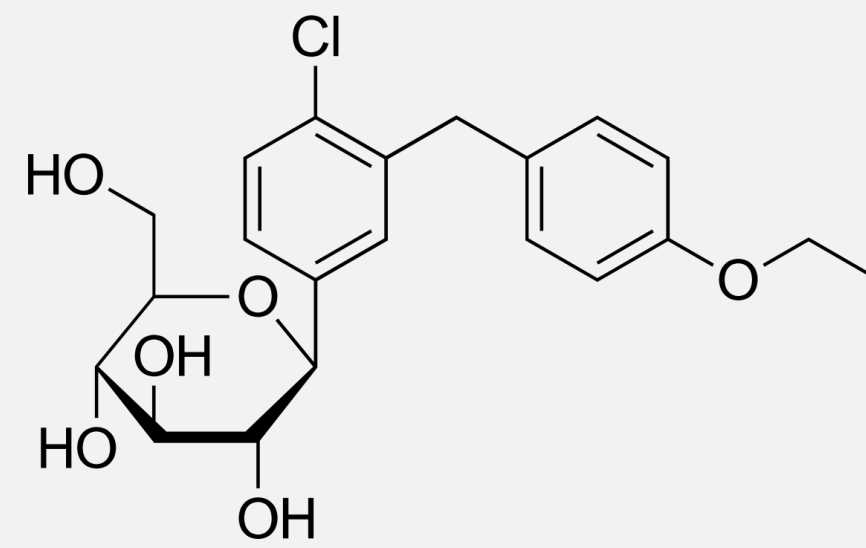


# Gliflozins Use in T2DM



## Abstract:

Gliflozins have been recently developed as an oral medication for the treatment of Type II Diabetes. They are SGLT2- Inhibitors which block the renal tubular reabsorption of glucose found in the blood and causes the glucose to be excreted through forced diuresis. The importance of this drug is that its mechanism of action is unlike that of other antihyperglycemic agents, in that it produces an insulin-independent lowering of the blood glucose levels. The drug was approved for the treatment of Diabetes Mellitus in 2013 but is still not yet approved for Diabetes Insipidus. Currently there are three Gliflozins approved by the FDA for the mono, dual and triple therapy of T2DM: Canagliflozin, Dapagliflozin, and Empagliflozin. As of present, Gliflozins are not a first-line treatment, but are instead given in adjunction to other medication, since the possible long-term side effects are still not entirely known, but they could possibly become an excellent treatment option for carefully selected patients in the future.

## Medical Use:

Mainly used for Diabetes Mellitus

Is **not** first-line of treatment

- Not very long safety record
- More expensive

Used for patients not responding to metformin monotherapy

- Especially useful to reduce weight

Usually used in dual therapy (Metformin/Gliflozin)

Can also be used in triple therapy

(Metformin/Gliflozin/Sulfonylurea)

Study reveals use of Gliflozin reduces death by 20% compared to placebo/no treatment

Evidence shows it also improves cardio-renal function in type 2 diabetes patients (dapagliflozin)

Canagliflozin promotes weight reduction and BP reduction

Indications: obese and hypertensive patients

Contraindications: pregnancy and renal insufficiency (GFR <45 mL/min)

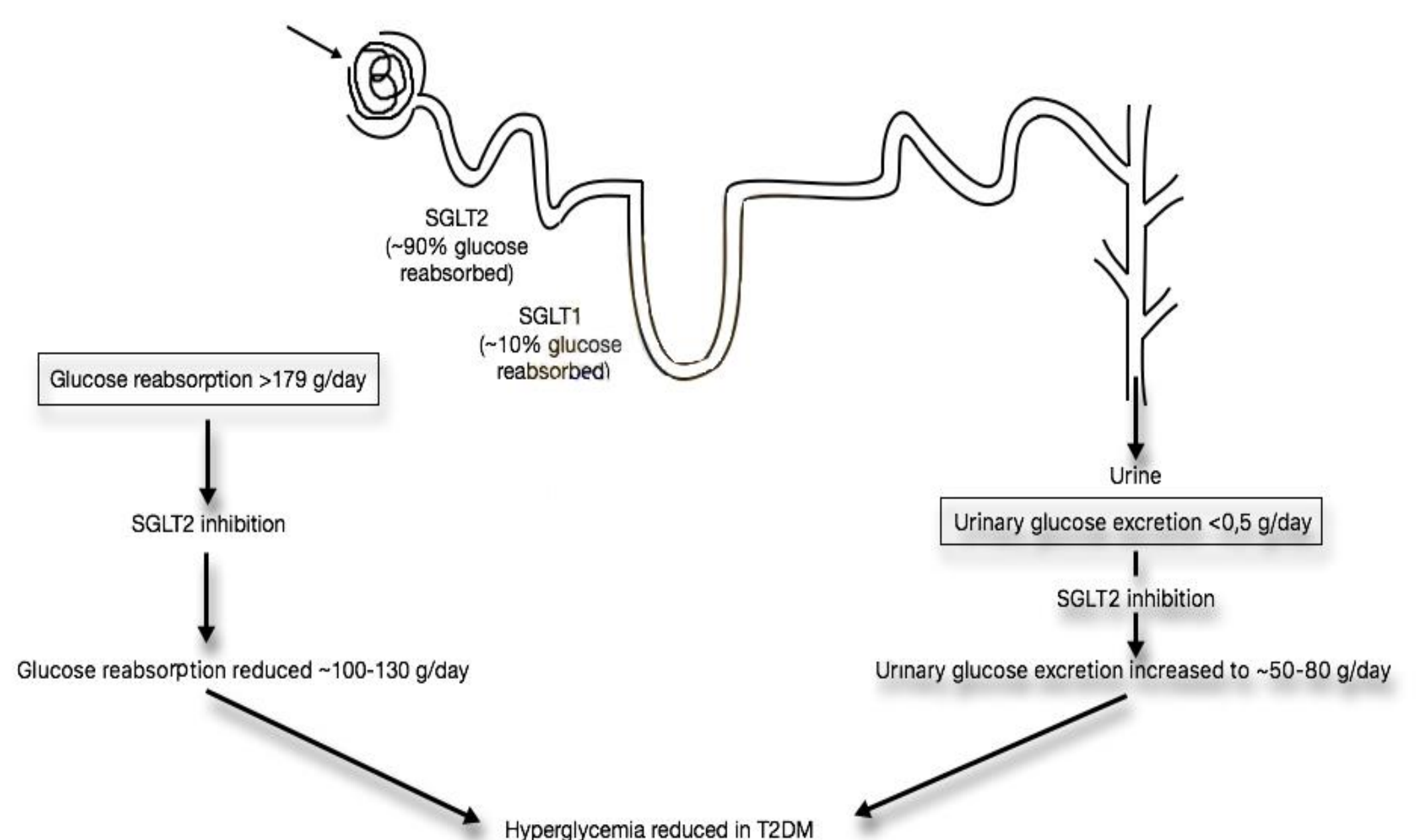
## Mechanism of Action:

SGLT2 → major transport proteins found in kidneys which maintains glucose balance in blood

- Mainly found in epithelial cells lining in proximal convoluted tubule
- Promote reabsorption from glomerular filtration back to blood (90% of reabsorption)

SGLT2 inhibitors block SGLT2 → inhibiting reabsorption of glucose into blood

- Glucose forced to be excreted through urine (forced diuresis)



[https://en.wikipedia.org/wiki/SGLT2\\_inhibitor#/media/File:Mechanism\\_of\\_action\\_.png](https://en.wikipedia.org/wiki/SGLT2_inhibitor#/media/File:Mechanism_of_action_.png)

## Side Effects:

Most commonly: genital & urinary tract infections (especially in women)

Rarely can lead to euglycemic diabetic ketoacidosis (euDKA) → especially perioperatively

Should only be given if patient is healthy, hydrated with balanced diet

Canagliflozin is associated with decreased mineral bone density → higher risk of fractures

Increased risk of:

- Lower limb amputation (especially toes) → due to decreased blood circulation
- Fournier gangrene
- Kidney injury
- Dehydration

Possibly teratogenic (contraindicated in pregnancy)

### References:

Hsia DS, Grove O, Cefalu WT. An update on sodium-glucose co-transporter-2 inhibitors for the treatment of diabetes mellitus. *Curr Opin Endocrinol Diabetes Obes.* 2017;24(1):73-79. doi:10.1097/MED.0000000000000311

Singh M, Kumar A. Risks Associated with SGLT2 Inhibitors: An Overview. *Curr Drug Saf.* 2018;13(2):84-91. doi: 10.2174/1574886313666180226103408. PMID: 29485006.

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<https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/sodium-glucose-cotransporter-2-sglt2-inhibitors#:~:text=SGLT2%20inhibitors%20are%20a%20class,canagliflozin%2C%20dapagliflozin%2C%20and%20empagliflozin>

<https://www.diabetes.co.uk/diabetes-medication/sglt2-inhibitors.html>

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