JPP April Tweetorial

Dapagliflozin

Day 1: In the mid 19thC, phlorizin extracted from the root bark of the apple tree was found to cause glycosuria; there was poor oral absorption & also, because non-selective, the inhibition of gut SGLT1 led to unpleasant gut side-effects. Synthesis of analogues in the 1990s led to [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin) licensed by EMA in 2012

Day 2 [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin): Indications are for primary diabetes mellitus as monotherapy (T2DM) or in combination with insulin for T1DM or T2DM. Dose 5mg (T1) or 10mg (T2) once daily. [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin) also routinely combined with other hypoglycaemic agents e.g metformin. NICE TA597 (2020) outlines strict guidance for [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin) use in T1DM, including BMI ≥27kg/m2 & providing education about ketoacidosis

Day 3: [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin); good oral absorption & bioavailability with high protein binding. Metabolised by phase 2 glucuronidation (minor CYP activity) with renal excretion of inactive metabolites- t½ 14hrs. Monitor renal function throughout & don't start if eGFR<60 60 mL/minute/1.73 m2 /avoid if <45

Day 4: MOA: the sodium glucose cotransporter 2 (SGLT2) manages ~90% of glucose reabsorption in proximal convoluted tubule. Inhibition of the transporter by [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin) leaves glucose in filtrate for excretion in urine. The calorie loss supports HbA1c reduction & weight loss. [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin) can affect urinary loss of an average of 300 calories/day. This translates to an average body weight loss of 2.7% (higher than for metformin)

Day 5: [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin) adverse drug events; common include genital infections, back pain, ketoacidosis (T1DM), dyslipidaemia, increased risk infection, urinary disorders. Uncommon are constipation, volume depletion, rarely Fournier’s gangrene. Low risk hypos (not exhaustive).

Day 5 (cont): Diabetic ketoacidosis with [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin) can occur in T2DM, but is only 'common' in T1DM. Putative pathway is lowered bl.glucose (SGLT2is) > reduced insulin, release of free fatty acids into citric acid cycle to ↑ energy & accumulation of acid by-products and metabolic acidosis. Risk factors for ketoacidosis include alcohol consumption, sub-optimal insulin dosing or increased insulin need, dehydration, caloric restriction

Day 6 : Drug-drug interactions for [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin); ‘moderate’ only & almost all are other hypoglycaemic agents having an additive effect, or drugs which have an additive hypotensive effect e.g amlodipine, bisoprolol

Day 7: Sodium, as well as glucose transport, is inhibited by SGLT2i’s such as [#dapagliflozin](https://twitter.com/search?q=%23dapagliflozin); therefore, less sodium is reabsorbed causing osmotic diuresis. The impact on circulating volume, BP, pre/afterload has cardiovascular benefits. Recent UK approval for heart failure (rEF)

CPD: in addition to the tweets, read the BNF sections on Diabetes, Type 2 diabetes and

and the monograph on dapagliflozin

Another useful source is the Summary of Product Characteristics for dapagliflozin– see links below

<https://bnf.nice.org.uk/treatment-summary/diabetes.html>

<https://bnf.nice.org.uk/treatment-summary/type-2-diabetes.html>

<https://bnf.nice.org.uk/drug/dapagliflozin.html>

<https://www.medicines.org.uk/emc/product/7607/smpc>

CPD questions (most but not all answers will be in the tweets). There is only one correct answer per question

1. Dapagliflozin is a chemical derivative from the cherry tree

TRUE or FALSE

1. Dapagliflozin was the first sodium glucose cotransporter 2 inhibitor (SGLT2i) to be licensed

TRUE or FALSE

1. Which of the following is TRUE?
2. You have to take dapagliflozin with food
3. Dapagliflozin cannot be combined with insulin
4. Dapagliflozin is a highly selective and potent sodium glucose cotransporter 2 inhibitor (SGLT2i)
5. Dapagliflozin is only licensed for use in type 2 diabetes mellitus
6. Dapagliflozin undergoes extensive phase 1 CYP450 breakdown

TRUE or FALSE

1. It is important to monitor renal function throughout use

TRUE or FALSE

1. Which of the following is FALSE?
2. Dapagliflozin mainly works in the proximal convoluted tubule
3. Sodium and glucose are both inhibited from reabsorption from dapagliflozin
4. Dapagliflozin usually has some weight loss effect
5. You should avoid initiating dapagliflozin if the eGFR is <80
6. The high concentration of glucose in the urine encourages urinary tract infections

TRUE or FALSE

1. Which of the following is NOT a risk factor for ketoacidosis?
2. Alcohol consumption
3. Has COPD as a co-morbidity
4. Dehydration
5. Missed insulin dose
6. Dapagliflozin has cardiovascular benefits

TRUE or FALSE

1. Dapagliflozin has multiple severe drug-drug interactions

TRUE or FALSE