CPD December 2022: Losartan

Day 1: After angiotensin converting enzyme inhibitor (ACEi) success, attention turned to the angiotensin II receptor (ATI) as a drug target. Discovery that anti-helminth medicines, the benzylimidazoles were weak antagonists, led to compound modification & production of a potent, selective agent [#losartan](https://twitter.com/search?q=%23losartan), licensed mid-1990s. This was 1st in class of now 8 ‘sartans’ in UK, also known as as angiotension II receptor antagonists (ATIIRAs), or angiotensin II receptors blockers (‘ARBs’)

Day 2: [#losartan](https://twitter.com/search?q=%23losartan) is licensed to treat hypertension in those over 6 yrs (including adults with stroke risk from left ventricular hypertrophy) dose 25-100mg o.d (lower range for elderly; child dose depends on body weight). Adults type 2 diabetes mellitus (T2DM) nephropathy 25-100mg; heart failure 12.5-150mg.

Day 2 [#losartan](https://twitter.com/search?q=%23losartan) (cont): 1st line anti-hypertensive for T2DM (all ethnicities) & those below 55yrs. BP lowering effect may be less in people of African origin so not 1st line; reason(s) remain unclear. Ethnicity not known to be relevant for use in other conditions e.g heart failure.

Day 3: [#losartan](https://twitter.com/search?q=%23losartan) kinetics; good oral absorption, low bioavailability, 1 hour to cmax. [#losartan](https://twitter.com/search?q=%23losartan) is a prodrug & CYP2C9 liver breakdown releases 1 active metabolite (CYP3A4 > inactive metabolites). Biliary & renal excretion. t½ 2-9 hrs. Caution/avoid depending on level renal/hepatic impairment

Day 4. Mechanism of action; in blocking the action of angiotensin II via AT1 receptors on blood vessels, kidney etc, [#losartan](https://twitter.com/search?q=%23losartan) impairs vasoconstriction & lowers BP, pre & afterload, as well as lowering salt/water retention. ARBs interfere less with RAAS system compared to ACEi drugs

Day 5 [#losartan](https://twitter.com/search?q=%23losartan) common adverse drug effects: renal impairment,hyperkalaemia (monitor K+ throughout use),nausea, vomiting. Uncommon:constipation, angioedema, myalgia, sleep disorder. Compared to ACEis, less likely to cause cough (no effect on bradykinin levels),or angioedema in African people. Symptomatic hypotension is common & one reason for ARBs included in the elderly STOPP (risk of syncope & falls) [#losartan](https://twitter.com/search?q=%23losartan) is not used in pregnancy (NOT EXHAUSTIVE)

Day 6: DDIs – do not use with ACEis (↑ risk renal impairment). Caution with any drug causing hyperkalaemia or hypotension; CYP2C9 inhibitors e.g fluconazole lead to less active metabolite so reduces drug action; NSAIDs can decrease BP lowering action & may increase risk of renal toxicity (NOT EXHAUSTIVE)

Day 7 The angiotensin receptor blockers are all five times less likely to cause angioedema in black African populations, compared to ACE inhibitors; therefore ARBs are considered a safer choice when appropriate

CPD: in addition to the tweets, read the BNF sections on ‘Drugs affecting the renin-angiotensin system’, and the monograph for Losartan, as well as the Losartan SPC

<https://bnf.nice.org.uk/treatment-summaries/drugs-affecting-the-renin-angiotensin-system/>

<https://bnf.nice.org.uk/drugs/losartan-potassium/>

<https://www.medicines.org.uk/emc/product/6004/smpc#gref>

1. The angiotensin receptor blocker (ARB) drug class is a derivative from anti-helminth medicines

TRUE or FALSE

1. There are now 5 ARB drugs on the UK formulary

TRUE or FALSE

1. Which of the following is TRUE?
2. Losartan can be used to reduce adult stroke risk if left ventricular hypertrophy
3. Losartan is licensed for use in all ages for hypertension
4. Losartan is licensed for heart failure in children
5. Adult start dose for hypertension is always 50mgs once daily
6. Losartan is useful in heart failure because it can reduce pre and afterload

TRUE or FALSE

1. Losartan is a prodrug

TRUE or FALSE

1. Which of the following statements is TRUE?
2. Asian and African ethnicities both have a sub-optimal response to losartan when used for hypertension
3. South Asian ethnicities respond poorly to all ARBs when used for heart failure
4. African populations are thought to respond less well to the antihypertensive effects of both angiotensin converting enzyme inhibitors and ARBs
5. Candesartan does not work for migraine in black African populations
6. Angiotensin receptor blockers are less likely to cause angioedema in all populations

TRUE or FALSE

1. The STOPP criteria in the BNF states two issues which could make an angiotensin receptor blocker ‘inappropriate’ for the elderly: persistent postural hypotension & hyperkalaemia

TRUE or FALSE

1. There are cautions when using an angiotensin receptor blocker with any drug which leads to hypotension

TRUE or FALSE

1. Which of the following is a ‘common’ adverse drug effect for ARBs?
2. Thrombocytopenia
3. Abdominal pain
4. Liver impairment
5. Arthralgia