# Dapagliflozine + Thiaziden M1168

| Onderbouwend | Stof | Effect | Code |
|---|---|---|---|
| EPAR Forxiga | dapagliflozine + HCT | toename 24-uurs Natrium-excretie in urine:<br>- dapagliflozine 35%<br>- hydrochloorthiazide % niet opgegeven<br>- dapagliflozine + hydrochloorthiazide (HCT): meer dan additieve toename, tov het effect van de afzonderlijke stoffen (→GIC: % niet vermeld).<br><br>p. 48 ev: there was a greater than additive increase in 24-h urinary Na+ excretion when single doses of dapagliflozin and HCT were co-administered, compared to either treatment administered alone. This may trigger/cause dehydration by leading to increased sodium loss and hyponatraemia with sequelae such as insufficient water intake, increase in haematocrit and potentially increased risk of thrombosis, particularly in elderly patients with an already decreased sense of thirst. | 1B |

| CTCAE | 1 = B | 2 = C | 3 = D | 4 = E | 5 = F |
|---|---|---|---|---|---|
| hyponatriëmie | <LLN-130 mmol/l | - | 130-120 mmol/l | < 120 mmol/l | dood |

| Overig | Stof | Effect |
|---|---|---|
| SPC Forxiga | dapagliflozine + bumetanide/ diuretica | Het werkingsmechanisme van dapagliflozine leidt tot verhoging van de diurese. Dapagliflozine kan het diuretisch effect van thiazide en lisdiuretica versterken.<br>Toename 24-uurs Na-excretie in urine:<br>- dapagliflozine 35%; bumetanide 108%;<br>- dapagliflozine + bumetanide 122% →GIC: som ≠ 35+108% |

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| EPAR Forxiga | dapagliflozine + bumetanide /diuretica | p. 48 ev: in healthy subjects 7 days of dapagliflozin administration increased 24-h urinary sodium by about 35%. Bumetanide alone had a larger effect (increasing by 108%). The combination of dapagliflozin and bumetanide had a transient (about 3 days) additive effect (maximum increase by 122%).<br>However, renal sodium loss may be even higher in patients with T2DM than in healthy volunteers due to the expected more pronounced dapagliflozin-induced diuresis. Combination with a loop diuretic may present a certain risk for clinically-meaningful electrolyte disturbances. In addition, the combination with bumetanide led to more pronounced (increase by 1.164 l on first day) and prolonged (9 days) renal fluid loss than either drug alone. This increase is considered substantial and the effect is maybe even more pronounced in patients with T2DM due to higher glucose load and consequently more pronounced osmotic diuresis. Particularly elderly patients with an already physiologically decreased sense of thirst may be at increased risk for dehydration.<br>Bumetanide transiently (10 days) decreased dapagliflozin-induced urinary glucose excretion which is not considered clinically relevant. The results also suggested that dapagliflozin may have modest effects upon systolic BP (up to 12 mm Hg reduction) alone or in combination with bumetanide in normotensive subjects.<br>Hypotension / hypovolaemia / dehydration were numerically higher in subjects that received a diuretic (either loop or thiazide) in combination with an ACE-inhibitor or ARB and received dapagliflozin compared with those that received placebo. |

**Opmerkingen**
PubMed, Hansten, Stockley: -

WFG: alleen voor thiaziden, niet lisdiuretica.

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| Risicogroep | |

| | **Interactie** | **Actie** | **Datum** |
|---|---|---|---|
| Beslissing WFG | Ja | Nee | 26 maart 2013 |