



MEMORANDUM

**FDA approves J&J's Invokamet (canagliflozin/metformin) fixed-dose combination - August 14, 2014**

**Executive Highlights**

- The FDA has approved J&J's Invokamet (canagliflozin/metformin), making it the first SGLT-2 inhibitor/metformin fixed-dose combination available in the US; the product is recommended for twice daily dosing, with a launch planned for August 18.
- Canagliflozin/metformin XR (which allows for once-daily dosing) is currently in development; an FDA decision on AZ's dapagliflozin/metformin XR combination is expected by 4Q14.

J&J just [announced](#) that the FDA approved its fixed-dose combination (FDC) of Invokana (canagliflozin) and metformin, which will be marketed under the brand name Invokamet in the US - the combination was recently [approved](#) in the EU as well, where its brand name is Vokanamet - both names have a nice ring to them. Invokamet will be dosed twice daily - different versions of the tablet will contain 50 mg or 150 mg doses of canagliflozin (for a total daily dose of 100 mg or 300 mg, the same daily dose as Invokana monotherapy) and 500 mg or 1,000 mg doses of metformin. It is indicated for type 2 diabetes patients that are not at their glycemic targets on a regimen containing metformin, Invokana, or metformin and Invokana taken as separate tablets.

Invokamet is the first SGLT-2 inhibitor/metformin FDC approved in the US, and the second such combination approved in the EU (behind AZ's [Xigduo](#), a combination of Forxiga [dapagliflozin] and metformin). AZ has a Xigduo XR FDC under review in the US, with a decision expected in 4Q14. That compound has the advantage of using the extended-release (XR) formulation of metformin, which will allow for once-daily dosing - all else being equal, many patients should perceive that as a significant advantage, both because of the convenience benefits - one co-pay and one pill, rather than two co-pays and two or more pills - and because, happily, metformin XR is associated with fewer GI tolerability issues. J&J's Invokana/metformin XR FDC remains in development in the US. We see Invokamet and other SGLT-2 inhibitor/metformin combinations as an excellent options to help tide patients over until SGLT-2/DPP-4 inhibitor combinations arrive on the market - J&J does not currently have a combination in that class, and the current leaders are Lilly/BI's empagliflozin/linagliptin (under review in the US) and AZ's saxagliptin/dapagliflozin (US/EU submissions expected by the end of the year) - promising phase 3 data on both candidates was presented at [ADA](#), demonstrating >1% A1c improvements. If SGLT-2 inhibitor/DPP-4 inhibitor combinations are priced using a sum-of-their-parts model, metformin FDCs would remain the more accessible option in terms of cost for many patients, depending on payer decisions (in the US in particular).

- **As a reminder, the FDA issued a CRL for Invokamet in November requesting additional data demonstrating that the twice-daily dosing regimen of Invokamet was comparable to that of the once-daily dosing of the approved Invokana single agent.** It was a fairly straightforward CRL, and the compound was re-submitted to the FDA earlier this year, as announced by J&J during its 1Q14 financial update.

-- by Manu Venkat and Kelly Close