Canagliflozin for the treatment of Type 2 Diabetes

Janssen's Response to the Appraisal Consultation Document

Following on from your letter dated 17th February 2014, please find below Janssen's response to the Appraisal Consultation Document (ACD).

Janssen believes that the ACD is a fair, balanced and thorough review of the original submission, the analyses conducted by the Evidence Review Group (ERG) and other supporting evidence. The recommendations for the use of canagliflozin in Type 2 diabetes mellitus (T2DM), as described in Section 1 of the ACD, are fully supported by the evidence. Janssen supports the recommendations, and we have no comments on Section 1 of the document. There are, however, two points within Section 4 that we would respectfully request that the NICE Committee considers:

Sections 4.3 and 4.7: Evidence for canagliflozin compared to sulfonylurea in dual therapy with metformin

Janssen understands the committee's view that sulfonylureas are not considered to be a relevant comparator to canagliflozin in dual therapy. We appreciate that this view is consistent with current clinical guidelines in the UK. Whilst we are content to accept the committee's view on this matter, Janssen does believe that it would be useful for NICE to include some commentary on the clinical and cost-effectiveness of canagliflozin versus sulfonylureas in section 4 for broader context. Whilst it was not considered directly relevant to the decision-making process, we do believe that the results of a direct, head to head comparison of canagliflozin against a standard of care agent in the UK should at least be referenced and reported in the FAD.

Section 4.10: Use of canagliflozin in combination with metformin and pioglitazone

Janssen agrees that pioglitazone is no longer routinely initiated in clinical practice However, there is a historical patient population that still receives pioglitazone and can thus be assumed to tolerate it. Janssen believes that the clinical evidence shows, that for patients who are failing on a regimen of metformin (MET) and pioglitazone (PIO), the addition of canagliflozin offers an effective treatment option. We therefore request that, within Section 4.10, the clinical and cost-effectiveness of canagliflozin in combination with MET plus PIO, as a treatment option for patients currently tolerating PIO who need added glycaemic control is discussed in more detail.

DIA3012 demonstrated that this combination can provide HbA1c reduction, weight loss and BP reductions (Figures 18, 21 and 24 of the original Janssen submission), similar to the reductions seen with canagliflozin in other combinations.

From a clinical perspective, fluid retention and risk of oedema with PIO (1) may be balanced by the diuretic effect of canagliflozin (2), thus making this a clinically useful combination and perhaps explaining to some degree the good efficacy seen in DIA3012, as presented in the original submission.

Additional Minor Comments

Section 4.17: 104 week data for canagliflozin

Two year data is presented in Figures 7, 9, 11 and 14 of the original manufacturer's submission to NICE. It is therefore requested that the following sentence is amended from:

"*The manufacturer clarified that although there were 4-year data for the DPP-4 inhibitors and GLP-1 analogues, only 52-week data were available for canagliflozin*."

To the following:

"*The manufacturer clarified that although there were 4-year data for the DPP-4 inhibitors and GLP-1 analogues, only 104-week data were available for canagliflozin.*"

Sections 3.32 and 3.33: incremental cost and QALY data not previously provided

The ICERs provided in Janssen's answers to the ERG Clarification Questions did not provide the incremental costs and QALYs for the comparisons described, and this was flagged in the ACD report in four instances as "costs and QALYs not provided". For completeness, these increments are given below, with the original sentence followed by the suggested revision with increments added.

Section 3.32

Please consider replacing the sentence:

"The ICER provided by the manufacturer at the clarification stage for the comparison with dapagliflozin was £2993 per QALY gained (incremental costs and QALYs not provided)."

With:

"The ICER provided by the manufacturer at the clarification stage for the comparison with dapagliflozin was £2993 per QALY gained (incremental costs £33; incremental QALYs 0.011)."

Please consider replacing the sentence:

Canagliflozin 100 mg continued to be less effective and less costly than a GLP-1 analogue after correcting the BMI data (incremental costs and QALYs not provided).

With:

"Canagliflozin 100 mg continued to be less effective and less costly than a GLP-1 analogue after correcting the BMI data (incremental costs -£2,414; incremental QALYs -0.034)."

Section 3.33

Please consider replacing the sentence:

"The ICER provided at the clarification stage for the comparison with dapagliflozin was £21,626 per QALY gained (incremental costs and QALYs not provided)."

With:

"The ICER provided at the clarification stage for the comparison with dapagliflozin was £21,626 per QALY gained (incremental costs £616; incremental QALYs 0.029)."

Please consider replacing the sentence:

"Canagliflozin 300 mg continued to be less effective and less costly than a GLP-1 analogue after correcting the BMI data (incremental costs and QALYs not provided)."

With:

"Canagliflozin 300 mg continued to be less effective and less costly than a GLP-1 analogue after correcting the BMI data (incremental costs -£1,879; incremental QALYs -0.018)."

References

1. Pioglitazone summary of product characteristics. http://www.medicines.org.uk/emc/medicine/4236. Accessed March 2014.
2. Original Janssen Submission references 1-4:
    - (1) Abdul-Ghani MA, Norton L, DeFronzo RA. Role of sodium-glucose cotransporter 2 (SGLT 2) inhibitors in the treatment of type 2 diabetes. Endocr Rev 2011 Aug;32(4):515-31.
    - (2) Cefalu W, et al. Efficacy and safety of canagliflozin versus glimepiride in patients with type 2 diabetes inadequately controlled with metformin (CANTATA-SU): 52 week results from a randomised, double-blind, phase 3 non-inferiority trial. The Lancet 2013 Jul 12;Published online.
    - (3) Chao EC, Henry RR. SGLT2 inhibition--a novel strategy for diabetes treatment. Nat Rev Drug Discov 2010 Jul;9(7):551-9.
    - (4) Wilding J., Blonde L., Chiasson J-L., Polidori D., Meininger G., Stein P. Canagliflozin Lowers HbA1c and Blood Pressure Through Weight Loss-Independent and Weight Loss-Associated Mechanisms - Poster presented at EASD. 2013 Sep 23; 2013.