From: [redacted]
Sent: 11 April 2014 13:24
To: TA Comm B
Cc: [redacted]
Subject: COMMENTS ON ACD: Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating anaemia in people having cancer treatment (including review of TA142) [ID541]
Attachments: A_100924_EMA_Binocrit outcome of PhVWP Sept 2010.doc; UPDATED CONTACT APRIL 2014 Appendix E - Participation and confidentiality (manufacturer consultee).doc

Dear NICE

We would like to commend you for an excellent appraisal of the evidence and welcome your recommendations to support the use of ESAs for treating anaemia in people having cancer treatment.

We have one comment only relating to the summary of adverse events as stated in section 3.4 in the ACD:

3.4 The summary of product characteristics for Eprex and Binocrit lists headache, nausea and pyrexia as very common adverse reactions
and deep vein thrombosis, hypertension, pulmonary embolism, diarrhoea, vomiting, rash, arthralgia and influenza-like illness as
common adverse reactions in patients with cancer. Stroke is also commonly seen with Binocrit. For full details of adverse reactions
and contraindications, see the summary of product characteristics.

The safety as well as the efficacy profile for biosimilars and their reference molecule are considered similar by the EMA.
Please note that the information regarding “stroke” was included in the PI (SmPC+PIL) in course of the renewal procedure for Binocrit finalised in 2012 due to a general request for all Epoetins from the PhVWP in 2010 (kindly refer to the attached document). This request concerned all Epoetins and was due to the results from the TREAT study concerning Darbepoetin alfa. DE presented the assessment of the results of the recently published clinical TREAT study showing that diabetic patients with CRF (chronic renal failure) and moderate anaemia are at increased risk for stroke when treated with darbepoetin alfa targeting Hb levels of 13 g/dL.
The findings of the TREAT study indicated that epoetins are not beneficial in diabetic patients with chronic renal disease suffering from moderate anaemia. It can be assumed that the effects are not limited to darbepoetin alfa. The findings from the TREAT study were considered as a class effect. Therefore, an amendment of the SmPCs (and PIL) for all epoetins was justified.
Please note that moreover the following centrally authorized Epoetins have also included the requested wording from the PhVWP in their PIs (Aranesp, Mircera, Neorecormon, Retacrit and Silapo) and there is no Sandoz specific deviation in this respect.
The reason why the EPREX UK SmPC and PIL has not been updated so far remains unclear to Sandoz. As EPREX is authorized via MRP there might be a delay in the SmPC update due to the different regulatory way of approval. Furthermore please note that the PRAC was not in place at the time of the recommendation from the PhVWP and this might also have influenced a delay in the local SmPC update.

Please do not hesitate to contact my colleague [redacted] should you require further clarification, copied in to this email.

Please also note the updated Sandoz contact details, attached, in relation to this appraisal.

Kind regards
xxxxxx

xxxxxxxxxxxxx
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