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|  | **Current text** | **Comment**  | **Suggested amendment**  | **RG comments** |
| **Text clarification** | *‘…however the RG note that patients recruited to the trial were not strictly* *treatment naïve as trial inclusion/exclusion criteria allowed for patients who had previously* *been treated with miglustat or ERT* ***within*** *6 or 9 months prior to randomisation.’* | This reads as though patients receiving active treatment with miglustat or ERT in the 6 to 9 months prior to the trial *were* eligible. From the ENGAGE pivotal study publication, ‘*Patients were eligible only if they had* ***not*** *received treatment with SRT within 6* *months or ERT within 9 months before randomization’ (Mistry et al 2015)* | *‘…however the RG note that patients recruited to the trial were not strictly* *treatment naïve as trial inclusion/exclusion criteria allowed for patients who had previously received miglustat or ERT****, but they could not have received treatment with SRT within 6*** ***months or ERT within 9 months before randomization****.’* | Suggest: Amend text. Suggest change ‘within’ to ‘up to’. The RG’s text ‘within’ was intended to be interpreted as ‘up to’ however the RG agree with applicant’s request to amend the text but suggest that the text reads as follows:*‘…however the RG note that patients recruited to the trial were not strictly* *treatment naïve as trial inclusion/exclusion criteria allowed for patients who had previously* *been treated with miglustat or ERT****~~within~~ up to*** *6 or 9 months prior to randomisation.* |
| **Text clarification** | *‘The aim of the study was to establish whether patients with GD1 whose disease was considered stable having reached* ***pre-specified therapuetic goals as defined by Pastores et al 2004*** *while receiving ERT for at least 3 years would remain stable after switching to eliglustat therapy. The ENCORE study provides evidence … ‘*  | This could read as though the Pastores defined therapeutic goals were the endpoints in the trial. The endpoints in the trial were defined specifically for the ENCORE trial. | *The aim of the study was to establish whether patients with GD1 whose disease was considered stable having reached* ***pre-specified therapuetic goals (Cox et al 2015)***  *while receiving ERT for at least 3 years would remain stable after switching to eliglustat therapy. The ENCORE study provides evidence**Or (note commas)* *The aim of the study was to establish whether patients with GD1 whose disease was considered stable****,*** *having reached pre-specified therapuetic goals* ***based on those*** *defined by Pastores et al 2004 while receiving ERT for at least 3 years****,*** *would remain stable after switching to eliglustat therapy. The ENCORE study provides evidence … ‘*  | **Not ammended**. The RG does not consider the addition of ‘based on those’ adds any further value in terms of a reader’s understanding of the text. Furthermore, the applicant had the opportunity to adress this during the FAC and failed to do this.  |
| **Text clarification** | *The applicant estimates the gross budget impact of eliglustat to be approximately* *€18,094,095 over 5 years.* | This reads as though the introduction of eliglustat would increase costs to the Irish system by €18,094,095 over 5 years. Using all the same assumptions the introduction of eliglustat into Ireland would **decrease costs by € 1,083,205 over 5 years**  | *The applicant estimates the* ***cost******of treating GD in Ireland with eliglustat as a treatment option would be approximately*** *€18,094,095 over 5 years.*  | **Not amended.**The RG was merely stating the gross budget impact of introducing eliglustat. The interpretation of the RG’s statement fails to consider the text which follows the statement being challenged by the applicant….’ The applicant estimates the gross budget impact of eliglustat to be approximately €18,094,095 over 5 years…….The costs included in the applicant’s budget impact analysis were linked with the cost utility model….. the applicant estimates that assumes a market share uptake of 56% in year 1 which translates as 5 patients being eligible for eliglustat therapy in year 1, increasing to 7 patients by year 5. The applicant also included direct medical and social service costs offsets from the introduction of eliglustat.’Taking into account the paragraph in its entirety, the RG hold the view that the paragraph addresses the applicant’s concerns. |

**References**

Mistry PK, Lukina E, Ben Turkia H, et al. Effect of oral eliglustat on splenomegaly in patients with Gaucher disease type 1: the ENGAGE randomized clinical trial. JAMA. 2015 Feb 17;313(7):695-706.

Cox TM, Drelichman G, Cravo R, et al. Eliglustat compared with imiglucerase in patients with Gaucher's disease type 1 stabilised on enzyme replacement therapy: a phase 3, randomised, open-label, non-inferiority trial. Lancet. 2015;385(9985):2355-2362.

Dear NCPE

For the purposes of clarity, Sanofi would like to draw your attention to the following minor factual inaccuracies which appeared in the final recommendation document as published on the NCPE’s website.