Errata to FDA Briefing Document

Genetic Metabolic Diseases Advisory Committee Meeting

August 2, 2024

This erratum contains corrections to FDA's Briefing Document for the August 2, 2024 Genetic Metabolic Diseases Advisory Committee (GeMDAC) Meeting. The committee will discuss the new drug application (NDA) 214927, submitted by Zevra Therapeutics for arimoclomol for the proposed treatment of Niemann-Pick Disease Type C.

1. Section 1.2, page 9/121 of the PDF says:

   "In the United States, miglustat is FDA approved for adults with Gaucher disease when enzyme replacement is not a therapeutic option."

   Revised text (additions in bolded and underlined font):

   "In the United States, miglustat is FDA approved for adults with Gaucher disease when enzyme replacement is not a therapeutic option. **Miglustat is also approved for co-administration with cipaglucosidase alfa-atga for the treatment of adult patients with late-onset Pompe disease.**"

2. Section 2.1, page 13/121 of the PDF says:

   "Miglustat is approved in the United States for adult patients with mild or moderate type 1 Gaucher disease (GD) when enzyme replacement therapy is not a therapeutic option."

   Revised text (additions in bolded and underlined font):

   "Miglustat is approved in the United States for adult patients with mild or moderate type 1 Gaucher disease (GD) when enzyme replacement therapy is not a therapeutic option. **Miglustat is also approved for co-administration with cipaglucosidase alfa-atga for the treatment of adult patients with late-onset Pompe disease**."

3. Section 3.1.1, page 16/121 of the PDF, the last sentence on the page says:

   "Subject-level data from an ongoing natural history study of NPC being conducted at the NIH and an Expanded Access Program sponsored by the Applicant under IND 214927 were also submitted and reviewed."

   Revised text (deletions in strikethrough font and additions in bolded and underlined font):

Subject-level data from an ongoing natural history study of NPC being conducted at the NIH and an Expanded Access Program sponsored by the Applicant under IND ~~214927~~ **124547** were also submitted and reviewed."

4. Section 3.1.3.2.3.1, page 24/121 of the PDF, the second paragraph says:

   "Regarding the analytical method for the R4DNPCCSS endpoint, the Applicant proposes to use an ANCOVA model including baseline miglustat use (yes/no) and baseline R4DNPCCSS score, which is different from the MMMR analysis prespecified for the protocol-defined 5DNPCCSS endpoint."

   Revised text (deletions in strikethrough font and additions in bolded and underlined font):

   "Regarding the analytical method for the R4DNPCCSS endpoint, the Applicant proposes to use an ANCOVA model including baseline miglustat use (yes/no) and baseline R4DNPCCSS score, which is different from the ~~MMMR~~ **MMRM** analysis prespecified for the protocol-defined 5DNPCCSS endpoint."

5. Section 3.1.3.3, page 33/121 of the PDF, currently says:

   "A clinical trial measurement approach that incorporates both the observable and non-observable aspects of swallowing dysfunction in NPC is consistent with NPC clinical management recommendations (Hong et al. 2021) and would have provided a more comprehensive picture of swallowing function in study subjects over time."

   Revised text (deletions in strikethrough font and additions in bolded and underlined font):

   "A clinical trial measurement approach that incorporates both the observable and non-observable aspects of swallowing dysfunction in NPC is consistent with NPC clinical management recommendations (~~Hong et al 2021~~ **Geberhiwot et al. 2018**) and would have provided a more comprehensive picture of swallowing function in study subjects over time."

6. Section 3.2.1, page 80/121 of the PDF says "Miglustat is approved for NPC in several non-US countries and approved for adults with GD in the United States."
   Revised text (deletions in strikethrough font and additions in bolded and underlined font):

   "Miglustat is approved for NPC in several non-US countries and ~~approved~~ **in the United States is** approved for adults with GD ~~in the United States~~ **and is also approved for co-administration with cipaglucosidase alfa-atga for the treatment of adults with late-onset Pompe disease**."