June 17, 2021

Dear NPC community,

This has been an especially challenging and disappointing time for the Niemann-Pick type C disease (NPC) community with Mallinckrodt's reporting of its failed trial of intrathecal (administration directly into the spinal canal) adrabetadex that reported no improvement compared to placebo, with a risk of hearing loss. We empathize with patients and families living with NPC, a serious, devastating disease that causes tremendous suffering and early death and that has no approved therapies. At a recent patient listening session and in letters and emails sent to FDA, we've heard first-hand from patients, caregivers, and investigators about the challenges they face, their commitment to the continued development of cyclodextrins like adrabetadex for NPC, their hope for continued access to adrabetadex, the need for multiple effective therapies, and the challenges with NPC clinical trials.

Although the FDA cannot comment publicly on specific drug development programs, we have a longstanding commitment to do all we can to further the availability and development of effective and safe drugs, particularly for conditions with unmet needs. We share a common goal with NPC patients, caregivers, drug companies and other stakeholders – to bring effective and safe treatments to patients as quickly and efficiently as possible. Well-designed and well-conducted clinical trials are the most efficient way to evaluate the safety and efficacy of drugs, and we are committed to working with stakeholders to facilitate the development of products for NPC and other rare diseases.

In situations where there are no satisfactory alternative therapies for a serious and immediately life-threatening condition, FDA provides a pathway for a patient to gain access to an investigational drug for treatment outside of clinical trials through expanded access, which is sometimes called compassionate use (https://www.fda.gov/news-events/public-health-focus/expanded-access). FDA authorizes expanded access if we determine that the potential benefits of the investigational drug justify the potential risks, the drug company is willing to provide the drug (we cannot require a company to provide its drug for expanded access), and this use does not interfere with drug programs that are intended to pursue approval for this use.

We are currently allowing expanded access to adrabetadex, when appropriate, if a company is willing to provide the drug. The decision to allow expanded access of adrabetadex takes into account that adrabetadex is injected into the spinal column every two weeks, that this procedure has associated risks, that adrabetadex can cause hearing loss, and the recent trial that reported adrabetadex to not be effective in the studied patient population. Based on these considerations, we are allowing expanded access for patients who are already receiving adrabetadex and appear to be benefiting, provided that the potential benefits justify the risks. We are also allowing expanded access for new patients who are in their first several years of life with infant-onset NPC and who have rapidly progressing neurological symptoms – a population that wasn't studied in the failed adrabetadex trial.

While expanded access provides important access to investigational drugs in certain situations, the goal with all investigational drugs is to determine in well-designed studies whether the drugs are, in fact, effective with benefits that clearly outweigh the risks. This is particularly challenging for rare diseases because the patient populations are small (which may impact the feasibility of certain studies), the natural history of the diseases are often not well understood (making it harder to optimally design clinical studies), and drug development tools such as established study endpoints are often lacking. Despite these challenges, we remain committed to working with all stakeholders to ensure that feasible, innovative, and well-designed trials are conducted to facilitate the development of treatments for rare diseases, including NPC.

Sincerely,

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