4/22/2021

Dr. Janet Woodcock
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Woodcock,

We write with utmost urgency regarding patient access to adrabetadex for Niemann-Pick Type C (NPC). We are some of the foremost experts on the disease and treat patients with this rare, degenerative and fatal disease. We write in support of intrathecal treatment with adrabetadex for children with NPC.

Leveraging research from NIH, Mallinckrodt had a development program for the medication, which they ended in January based on negative results in their phase 2/3 trial, although allowed ongoing treatment for patients in an open label treatment program until October 2021, to give patients an opportunity to transition. Many of the children who were in the trial have access to adrabetadex through an open label extension and many others through an expanded access program (EAP), but there are children who need access to the drug now. We cannot get permission from your Agency to enroll them in the EAP.

For example, one child, Woodrow, is beginning to display significant neurological symptoms. We know that within the upcoming months, he will lose previously gained milestones, after which his developmental potential will never be the same: he will likely never talk, walk or even swallow. However, if we give him adrabetadex right now, we can stop or slow the progress of NPC and potentially stabilize him, giving him a chance at ongoing development, as we have seen in other young children treated with intrathecal adrabetadex. There are at least two other children in similar circumstances.

As scientists, we believe firmly that data about these children's status, progress and degeneration should be recorded, studied and shared. While we design and get approval of a protocol for a case-control study suggested by FDA - a process which could take three to six months - children like Woodrow cannot wait.

The data on adrabetadex are still being analyzed. However, we have seen dramatic results in many cases. Two sibling pairs with early and late adrabetadex treatment show a stunning difference in regression. We have seen that young children - 4 years old or younger - did not just stabilize, but made developmental progress and, in some cases, have normalized after IT adrabetadex therapy. Those with symptoms by age 2 who did not get treated deteriorated rapidly over the next year, as is typical of the early onset disease.

The official notice from Mallinckrodt regarding the trial of adrabetadex mentions adverse events; however, we have not seen evidence of adverse events beyond hearing loss, which is also caused by NPC. Hearing loss can be controlled by increasing the dose gradually, and can be mitigated by technologies such as hearing aids. The effects of NPC, however, cannot be mitigated at all.

We understand that FDA has been denying expanded access to children with NPC. **We request that you officially confirm your acceptance of children beginning treatment through EAP, and remaining on adrabetadex at this time, while we work to establish a new development program by October 2021.** We promise to make these children a part of ongoing case-control studies to scientifically give definitive answers to questions regarding the efficacy of intrathecal adrabetadex in this population. We will be better able to document the effects of the treatment the earlier we are able to start it in early onset patients, making our studies more robust.

As researchers and medical providers, we have taken an oath to do no harm. We strongly believe that ending treatment of adrabetadex and withholding it from potential patients is harmful. Please help us help these children.

Signed,

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