

Attachment #5

Subject: Re [redacted] (Nutropin Depot)
Date: 5/12/2003 1:48:45 PM Eastern Daylight Time
To: [redacted] (MD)

just received the copy of the report. It looks like 6 case reports of diabetes on Nutropin depot.
1 yr old boy x2 (same case or 2 different?)
8 mo girl
1 yr old girl
0 yr old and unspecified age girl (both [redacted])

The boy is listed as having diabetes Mellitus aggravated, which I could interpret as implying that the Nutropin aggravated (worsened) his preexisting diabetes or seemed to precipitate ketoacidosis, which is different than if he is a new case of diabetes. Do you have a different idea about what aggravated might mean?

According to Dr Wagner, there were no other Turner girls who got diabetes on Depot, so the 9y and 18m girls must be non-Turner.

On the other hand, if these are four new cases on Depot I am curious as to the total number of children treated with Depot. The incidence of type 1 diabetes is about 1 in 400 children by age 21, with most of the risk between 2 and 16 years. The annual type 1 risk might be about 1 in 6000 children in the 2-16 yr old general population. The key numbers are how many cases of type 1 diabetes have occurred in how many patient years of treatment with Depot. If the first number is 4, the second would have to be at least 20,000 for the diabetes to be coincidental.

Perhaps the major issue here is not a special risk with Turner compared to other girls, but Depot in anyone compared with other forms of GH.

I won't go to the ncgs investigator's meeting this past year, but plan to go this coming september. I will ask for a review of diabetes cases specifically on Nutropin Depot.

>>> [redacted] 05/12/03 10:53AM >>>
Dear DR

Thank you. Your analysis is, I'm sure correct, in this matter. After you receive and review the data report I sent you from CDER regarding adverse events to Nutropin Depot, I'm hoping we could have a short review of it's contents. It appears to me that, although Genentech was not required to report the onset of [redacted] diabetes in a expedited(15-Day) report, I believe they are mandated to report the occurrence in their periodic reporting. A review of the data report indicates that they didn't report it, and haven't submitted a periodic report since 08/03/01. These reports are required quarterly initially and subsequently, yearly. Please advise me of your conclusions after you have an opportunity to review the data report. Thank you [redacted]

----- Headers -----