

Hunter Syndrome/MPS II – FDA-Requested Listening Session

February 4, 2020

Objectives of session

- Learn about the Mucopolysaccharidosis Type II (MPS II), or Hunter syndrome, symptoms and how patients/caregivers currently manage their symptoms.
- Understand how the symptoms have progressed over time.
- Understand what aspects of the disease are important for a medical product to address.

Discussions in FDA Listening Sessions are informal and not meant to replace, but rather complement existing patient engagement opportunities in the Agency. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report summarizes the input provided by patients and those representing patients with MPS II at the meeting. To the extent possible, the terms used in this summary to describe specific manifestations of MPS II, and the health effects and impacts, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire MPS II patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.

Summary of the discussion by question

1. Of all the symptoms that your child experiences because of MPS II, can you tell us which symptom has the greatest impact on your child's life and in what way?

- A majority of the caregivers said cognitive delay is the most burdensome symptom experienced. This includes communication and adaptive skills. Some of the impacts described as a result of this symptom include a short attention span, impulsive behavior, irritability or aggression, and the constant need for attention.
- Another burdensome symptom includes tight muscles and/or tendons. Particularly, caregivers mentioned some patients are unable to raise their hands above their heads. Some patients received calf lengthening surgery and carpal tunnel surgery as a result of the tightness. Caregivers shared that the patients are unable to physically keep up with their peers or siblings when playing or running.

2. When thinking about the most burdensome symptoms your child experiences, can you describe what improvement would look like to you?

- Nearly all caregivers indicated that improvements in communication would signify improvement. This includes saying "hello," writing, communicating at an age-appropriate level, and interacting and playing with siblings and/or peers. Caregivers shared that they want patients to not only communicate with them, but also with others. They want them to be able to communicate when they are in pain or when they need to use the bathroom. Showing emotion appropriately, improved focus, and less outbursts could also be indicative of improvement.
- Caregivers also described improvement as patients becoming self-sufficient and independent. This was defined as the ability to care for their basic needs, including being potty-trained and performing daily routines such as brushing their teeth, using the

bathroom, putting on shoes and taking showers independently. Caregivers expressed that improvement would also include patients participating in mainstream education.

3. Are there specific activities your child cannot do as fully as you would like because of MPS II?

- A majority of caregivers indicated that patients cannot focus or maintain eye contact. Caregivers shared that patients are hyperactive, impulsive, and unable to self-entertain. Some caregivers shared that it is difficult for patients sit through a movie, sit down so they can be read to, and play with other kids. Most patients are unable to participate in activities because of their limited ability to focus and communicate.
- Caregivers also described physical limitations, such as joint stiffness and muscle pain, which limits patients' mobility. Some patients utilize braces to help with calf muscles. Particularly, some caregivers indicated that patients do not have a full range of motion in their knees, fingers, and hands. Consequently, patients experienced difficulty playing with toys and structures at the playground. Some patients are also unable to zip zippers, button buttons, tie shoes, or play any sports. Caregivers added that that simple tasks like gripping eating utensils or pressing icons on an iPad become increasingly difficult for patients.

4. How has your child's condition and symptoms changed over time?

- Most parents indicated that patients' symptoms either plateaued or worsened over time. Caregivers added that patients also plateaued in their learning ability and decreased in ability to control their body. Caregivers shared that patients developed hearing loss over time. Patients experienced worsening of attention span, hyperactivity, and memory loss. The impact of decreased body control includes being accident-prone and not being able to use the toilet, resulting in the use of diapers.
- Other caregivers indicated regression in patients' health condition. Caregivers shared that patients developed mild mitral valve leakage and required surgical procedures such as umbilical hernia, carpal tunnel, and tendon repair. Caregivers added that patients' joints progressively worsened.
- The few caregivers that reported improvements in symptoms shared that patients were more focused after medication dosing and did not suffer any adverse changes in their heart condition. One caregiver added that the patient was able to run and climb, and felt the patient was not progressing negatively.

5. How well does your child's current treatment regimen treat the most significant symptom/s of MPS II?

- All caregivers indicated that Enzyme Replacement Therapy (ERT) has or will be used to treat symptoms of MPS II. Nearly all caregivers mentioned using physical, occupational, and/or, speech therapy to also treat symptoms of MPS II.

- All caregivers who have used ERT for treatment reported improvements in patients' symptoms. Caregivers described the following improvements in patients while on ERT: decreased abdomen size, normalized liver and spleen, improved skin, hair, nails and facial features, improved comprehension and focus, cessation in deterioration of the heart, increased stamina, decreased sinus colds, and reduced incidental self-inflicted injuries.
- When considering how their child's condition and symptoms have changed over time, a majority of parents indicated that their child's condition has either plateaued or regressed in most areas.

6. Would you be willing to accept severe or life-threatening risk in order to gain improvement in your child's disease? Please explain why or why not.

- A majority of caregivers indicated they would be willing to accept severe or life-threatening risks. Four of the seven people who said this specifically acknowledged that the prognosis of the disease is death if left untreated; therefore, they are open to the opportunity. One caregiver indicated that it would "depend on what the treatment was and how high the risk was." Another caregiver characterized it as the "lesser of two evils."

7. Would you participate in a randomized clinical trial, given there is a possibility your child may receive the placebo? Please explain why or why not.

- Three caregivers indicated they would only participate in a randomized clinical trial if it were the only option available. Among the three, one of the parents added that the duration of the trial would depend on the site location and how often the child would be treated or tested.
- Four caregivers said they would not participate in a clinical trial where the possibility exists for their child to receive the placebo. One caregiver stated that doing so sacrifices the already limited amount of time the child has to live.
- One caregiver indicated it would "depend on the science," adding they participated in a trial in the past but would not participate at the moment because it does not have a high probability of being effective and would exclude the patient from other clinical trials.

8. Additional comments:

- Some caregivers emphasized the importance of early testing for MPS II, reasoning that early diagnosis has a significant impact on patients' quality of life.
- Some caregivers stressed that time is of the essence while requesting the FDA work to discover new treatments and cures, and approve new trials.
- Some caregivers expressed disappointment with narrow study criteria that results in patients' ineligibility for trials.

Partner organizations

The National Organization for Rare Disorders (NORD) helped identify and prepare patient community participants.

The Reagan-Udall Foundation for the FDA assisted with producing the summary of this meeting.

NORD and the Foundation were present during the listening session.

FDA division represented

- Office of the Commissioner, Patient Affairs Staff (organizer)
- Center for Drug Evaluation and Research (CDER), Division of Gastroenterology and Inborn Errors Products (DGIEP)
- Center for Biologics Evaluation and Research (CBER), Office of Tissues and Advanced Therapies (OTAT)

Patients and caregivers represented

7 caregivers participated in the listening session representing 9 MPS II male patients, including two sets of siblings.

- Patient ages ranged from 2 months to 12 years old.
- 2 patients were currently enrolled in a clinical trial.
- All patients received ERT, with the exception of 1 who was planning to receive ERT.
- Nearly all patients experienced regression in symptoms.
- Age of onset varied with four patients diagnosed at age 2, two patients diagnosed at age 3, one patient at age 7, and one patient at 6 weeks old.

Prior to the Listening Session, caregivers shared:

- Burdensome symptoms: Behavioral issues, communication/speech challenges, enlarged liver or spleen, heart issues, hearing loss, joint issues, and difficulty with movement.
- Management of MPS II and/or its symptoms: Enzyme Replacement Therapy, physical, speech, behavioral, and/or occupational therapy, hearing aids, medication, carpal tunnel surgery, tonsillectomy, leg braces, and Botox injections.

Financial Interest

- More than 1 caregiver indicated they may have a financial interest, but they are not receiving compensation for participation or attendance in this listening session.