July 28 ,2018

Dear SMA Community,

In response to your request, we would like to provide you with the following information and address your questions and concerns about the upcoming SPINRAZA (nusinersen) EU label (Prescribing information and Package Leaflet) update that will include information on the potential risk of hydrocephalus.

All medicines are evaluated for the benefit they provide to patients as well as the potential side effects and risks which may occur. With increased use, it is common and not unusual for medication labels to be updated. Right now, the benefit-risk profile for nusinersen remains unchanged and positive. Importantly, it has not been established that hydrocephalus has been caused by nusinersen, and no cases of hydrocephalus have been observed in the nusinersen clinical studies. Therefore, this update has not restricted use of nusinersen for any age or type of SMA.

With over 5,000 patients treated with nusinersen worldwide, ongoing patient safety remains of the utmost importance for Biogen. We would like to reassure you that we will continue to monitor and evaluate adverse events (AEs) and safety data for individuals with SMA treated with nusinersen and report to the local regulator/health authority in accordance with regulations.

For further information, please refer to your treating physician and/or SMA Europe http://www.sma-europe.eu/. Biogen will continue to be available to provide any further updates if requested.

Best regards,

The SMA Biogen Team

Additional Questions and Answers

What is hydrocephalus?

Hydrocephalus is a disorder where there is a build up of too much fluid called cerebral spinal fluid (CSF) in the brain. This can lead to an increase in pressure inside the skull. Possible signs and symptoms of hydrocephalus include persistent vomiting or headache, unexplained decrease in consciousness, and in children, an increase in head circumference.

The condition typically requires urgent neurosurgical intervention and may be treated with the placement of a shunt which helps drain the excess cerebral spinal fluid from the brain.

Does treatment with SPINRAZA cause hydrocephalus?

It has not been established that hydrocephalus has been caused by nusinersen, and no cases of hydrocephalus have been observed in the nusinersen clinical studies. Therefore, this update has not restricted use of nusinersen for any age or type of SMA. We would like to reassure you that we will continue to monitor its safety in ongoing clinical trials and the post-market setting.

Why did the EMA add this update now? Why is it already listed in labels in other countries?

The EMA reviewed the relevant post-market data and concluded that the topic should be added to the Warnings and Precautions. The U.S., Switzerland, Brazil, Canada and Australia have previously added information regarding the risk of hydrocephalus to their labels. In general, labeling differences between regulatory authorities may be due to several factors such as review processes with varying data requirements and interpretations of data including the amount of data available at the time of submission.

(note: *Always refer to your local country version of the PI/ SmPC, particularly regarding communication of Warnings & Precautions, "black box" warnings, "black triangle" language, or similar requirements for additional monitoring.)*

When did Biogen learn of the cases and how many have been reported? What can you tell us about them?

As of July 6, 2018, there have been five reported cases which were identified in the post-marketing setting, following the first global approval in December 2016. No cases of hydrocephalus were observed in clinical trials. We are continuing to seek updated information on these cases for ongoing evaluation and will continue to share information with regulatory bodies as appropriate. Due to patient confidentiality, we are not able to provide information on specific patients.

Has EMA restricted the SPINRAZA label?

No. The benefit-risk profile of nusinersen has not changed and there is no change in who can be prescribed nusinersen.

How is the information being shared with clinicians?

Letters to treating physicians are sent to keep them informed about updates to important prescribing information. In agreement with local authorities, we will be sending a letter to EU physicians who treat patients with SMA.