SPINRAZA™ (nusinersen) EU label (Prescribing information and Package Leaflet) has been updated to include information on reports of hydrocephalus in patients treated with nusinersen.

Patient safety remains of the utmost importance for Biogen. We will continue to collect more information on hydrocephalus in patients treated with nusinersen, and to monitor and evaluate adverse events (AEs) and safety data for individuals with SMA treated with nusinersen.

The benefit-risk profile for nusinersen remains positive for the treatment of SMA.

Dear Board Members of SMA Europe,

In response to your request, we would like to provide you with further information about the upcoming change to the SPINRAZA (nusinersen) EU label (Prescribing information and Package Leaflet), that will include a warning regarding the possible risk of hydrocephalus.

With more than 5,000 patients treated with nusinersen worldwide, ongoing patient safety remains of the utmost importance for Biogen. All medicines are continuously evaluated for the benefit they provide as well as the potential side effects and risks which may occur. With increased use, medication labels are updated as new information becomes available. In November 2017, in parallel with submissions to other Regulatory Authorities in countries where nusinersen has marketing approval, Biogen submitted to the European Medicines Agency (EMA) an application to update the product label with information about reports of hydrocephalus.

Biogen has received and evaluated reports of hydrocephalus in patients treated with nusinersen which indicates that it is a potential risk of treatment. The benefit-risk profile for nusinersen remains positive for the treatment of SMA. No cases of hydrocephalus have been observed in the nusinersen clinical studies to date. We will continue to evaluate the possible risk of hydrocephalus in patients treated with nusinersen as new information becomes available. This update has not restricted use of nusinersen for any age or type of SMA.

On the 12th July 2018, the EMA recommended the approval of the inclusion of hydrocephalus to the EU label, and we anticipate formal approval by the EU Commission within the next few months. Upon approval by the Commission, information on the reports of hydrocephalus will be included under the "Warnings and Precautions" and "Possible side effects" sections of the package leaflet and corresponding sections of the label ("Special Warnings and Precautions" and "Post-marketing experience"). The request to add this possible risk to the label has been approved in other countries (US, Australia, Canada, South Korea, Brazil, Switzerland).

It is important to note that the process for implementing this update follows specific requirements of the applicable Regulatory Authorities. Providing timely information to doctors and other healthcare professionals is of paramount importance whenever new safety information emerges. Biogen, in agreement with the EMA and the National Competent Authorities, has sent a letter to physicians involved in the care of SMA patients (such as neurologists and neuropaediatricians). This communication informs them about the reports of hydrocephalus in nusinersen treated patients, provides details on possible signs and symptoms, and guidance on what to do if they suspect

hydrocephalus. Some National Competent Authorities publish related information on their website in the local language which may provide further information.

Hydrocephalus is a disorder where there is a buildup of too much fluid called cerebrospinal fluid (CSF) around the brain. This can lead to an increase in pressure inside the skull. Possible signs and symptoms of hydrocephalus include increase in head size (in children), unexplained decreased consciousness, and/or persistent vomiting or headache.

The placement of a shunt which helps drain the excess CSF from the brain may be required in patients with hydrocephalus. The benefits and risks of continuing nusinersen whilst having a shunt in place are not known.

Physicians are advised to discuss this possible risk with patients/caregivers and advise them to be aware of signs and symptoms of hydrocephalus. If you have any questions or concerns, please contact your treating physician.

It is not typical or appropriate to disclose details of any ongoing discussions with Regulatory Authorities. Additionally, maintaining and protecting patient confidentiality is an obligation of utmost importance. As appropriate, Biogen will continue to be available to provide any further updates if requested.

Biogen is committed to supporting patients and families being treated with nusinersen throughout their treatment experience. Patient Support Programs are offered in select countries to provide participants with individual advice and information, with the overall goal to mitigate additional burden of treatment with nusinersen. Patients can raise both general questions about the treatment as well as reflect on the individual treatment experiences. Should an adverse event be reported, the details are shared with the Biogen safety department for assessment. We will continue to report additional safety information to the EMA and other applicable Regulatory Authorities in accordance with regulations.

We remain committed to continuing to work closely with patient organizations to best support the informational needs of the SMA community in a helpful and transparent manner.

For further information, please refer to your treating physician.

Best regards,

The Biogen SMA Team

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