



Dear Rett Syndrome community,

You may have seen in recent news that on Tuesday, August 6, 2019, the FDA released a statement addressing data concerns with the application for the approval of Zolgensma® (onasemnogene abeparvovec-xioi), a gene therapy currently on the market for patients less than 2 years of age with spinal muscular atrophy (SMA). The FDA as well as AveXis supports the continued use of Zolgensma due to the totality of evidence supporting its overall safety and effectiveness. We have and will continue to work in close cooperation with the FDA to appropriately update our submission and address any identified quality gaps. We remain fully confident in the safety, quality and effectiveness of Zolgensma.

Due to the data integrity concerns related to a specific animal testing procedure used in the development of Zolgensma and included in the application, we have decided to also review data quality and compliance with the preclinical work performed for AVXS-201, our Rett Syndrome gene therapy candidate. Out of caution, and to ensure that we have a robust data package for the FDA we have chosen to repeat and add additional pivotal preclinical studies as well as new quality controls. Once these studies are completed, we will submit the revised IND (investigational new drug application) to the FDA with the goal of rapidly progressing to clinical trials in Rett Syndrome patients. We expect that conducting these additional studies and completing the IND will take until the middle of 2020. At that time we will be in a position to provide further updates to the Rett Syndrome community.

We recognize that this news will cause concern and disappointment. Please know that AveXis remains focused and steadfast in our commitment to the Rett program and to ensuring the highest levels of transparency and integrity with the patients and providers we serve, and health agencies.

“Rett Syndrome continues to be a key focus for AveXis and we maintain a high sense of urgency to progress clinical studies for AVXS-201. We look forward to serving as a trusted member of the Rett Syndrome community and partnering with patients, advocates, physicians and regulators as we work to better understand the clinical impact of gene therapy for this devastating disease.” –

Dave Lennon, President of AveXis

We also wanted to share that Page Bouchard, DVM has been appointed Senior Vice President of Research and Chief Scientific Officer, AveXis, effective August 5, 2019. Dr. Bouchard is a 27-year industry veteran with experience in well over 100 Investigational New Drug programs and dozens of New Drug Application/Biologics License Application filings. He has been with Novartis for 10 years and most recently was the Global Head of Preclinical Safety for Novartis Institutes for BioMedical Research (NIBR). He is leading the management team responsible for our Rett program.

Sincerely,

The AveXis Team

Indication and Important Safety Information for ZOLGENSMA® (onasemnogene abeparvovec-xioi)

What is ZOLGENSMA?

ZOLGENSMA is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into the vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

What is the most important information I should know about ZOLGENSMA?

- ZOLGENSMA can cause acute serious liver injury. Liver enzymes could become elevated and may reflect acute serious liver injury in children who receive ZOLGENSMA.
- Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function.
- Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, or if the patient misses a dose of the corticosteroid or vomits it up.

What should I watch for before and after infusion with ZOLGENSMA?

- Viral respiratory infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see signs of a possible viral respiratory infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.
- Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if a patient experiences unexpected bleeding or bruising.

What do I need to know about vaccinations and ZOLGENSMA?

- Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid.
- Protection against respiratory syncytial virus (RSV) is recommended.

Do I need to take precautions with the patient's bodily waste?

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

What are the possible or likely side effects of ZOLGENSMA?

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

The safety information provided here is not comprehensive. Talk to the patient's doctor about any side effects that bother the patient or that don't go away.

You are encouraged to report suspected side effects by contacting the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch, or AveXis at 833-828-3947.

Please see the [Full Prescribing Information](#).

Attachment

[Novartis media release - ZOLGENSMA FDA update - August 2019.pdf](#)