Dear SMA community,

On Tuesday, August 6, 2019, the FDA released a statement addressing data concerns with the application for the approval of Zolgensma® (onasemnogene abeparvovec-xioi). First and foremost, AveXis is fully confident in the safety, quality, and effectiveness of Zolgensma. The FDA as well as AveXis supports the continued use of Zolgensma for patients with spinal muscular atrophy (SMA) less than 2 years of age due to the totality of evidence supporting its overall safety and effectiveness.

On June 28, AveXis notified the FDA that some data previously submitted to the agency as part of our approval application was inaccurate. The test in question was used for early animal testing for product potency and was discontinued in June 2018. When these concerns about data manipulation in a specific animal testing procedure were brought to our attention by an AveXis associate in mid-March, an independent investigation with the support of external counsel was immediately started to rapidly understand any implications and address the situation. In early May, the first part of our investigation confirmed discrepancies in the data and raised data integrity concerns. We then launched the second part of our investigation - a full technical quality investigation through our standard operating procedures to determine what, if any, updates would be required to regulatory filings. We concluded our investigation on June 27th and notified the FDA on June 28th.

“Upon becoming aware of the allegations, we worked quickly to conduct a robust investigation that was science-based and patient-driven. At no point throughout the investigation was there any indication that the findings impacted the safety, effectiveness or quality of Zolgensma Therefore, we followed the principle of completing our investigation and then communicating an accurate and complete assessment of the findings to health authorities. We determined that the potential data issue in question impacted a very small amount of data and did not impact the product's overall favorable benefit-risk profile. Once we completed our investigation, we shared our findings with the FDA.” – Dave Lennon, President AveXis.

AveXis is committed to taking appropriate action to prevent future incidents. We are in the process of exiting the small number of AveXis individuals involved in these data inaccuracies. We do not believe this issue extends beyond these individuals and does not impact our clinical data or our gene therapy platform.

We recognize this news may have caused concern among the community and we want to reinforce our commitment to ensuring the highest levels of transparency and integrity with the SMA Community, the patients and providers we serve, and health agencies. We do not expect this situation to impact the timing of our ongoing

SMA development programs and we will continue to keep the SMA community updated and informed. We plan on hosting a webinar with Cure SMA in the next couple weeks to provide the community with additional updates related to Zolgensma.

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