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Community Statement from Novartis Gene Therapies: Zolgensma Safety Monitoring Update on Acute Liver Failure

Dear SMA Community,

Novartis Gene Therapies is committed to patient safety and the ongoing monitoring of adverse events as it relates to the use of Zolgensma® (onasemnogene abeparvovec-xioi), gene therapy for spinal muscular atrophy (SMA).
The media reported about two patient fatalities related to acute liver failure in Russia and Kazakhstan in the weeks following Zolgensma dosing, during the corticosteroid taper. While hepatotoxicity including acute liver failure is an important known potential risk highlighted in the Zolgensma labeling, including the Boxed Warning in the U.S. Prescribing Information, these are the first fatal cases related to acute liver failure. As such, in alignment with health authorities, we will be updating the Zolgensma labeling to specify that fatal acute liver failure has been reported.

We are deeply saddened by the passing of these children, and our thoughts are with their families.

While this is clinically important safety information, it is not a new safety signal and we firmly believe in the overall favorable risk/benefit profile of Zolgensma, which to date has been approved in more than 40 regions and countries worldwide and has been used to treat more than 2,300 patients worldwide across clinical trials, managed access programs, and in the commercial setting.

We have notified health authorities in all countries where Zolgensma is used and are communicating to relevant healthcare professionals as an additional step in markets where this action is supported by health authorities. Additionally, communications distributed to prescribers stress the importance of enhanced monitoring of liver function during the corticosteroid tapering period, and for at least three months after Zolgensma infusion, and/or at other times as clinically indicated.

Zolgensma continues to be available and ongoing clinical trials are not impacted. We remain committed to Zolgensma and to you, our valued SMA community. Should you have any additional questions, please contact us at medinfo.gtx@novartis.com, by phone at +353 1 566 2364 (Monday to Friday, 9AM – 5PM CET), or via our medical information website (https://medinfo.novartis.com/gene-therapies/).

The current Zolgensma patient information leaflet can be found via the following link https://www.ema.europa.eu/en/documents/product-information/zolgensma-epar-product-information_en.pdf

Sincerely,

Theodora Weisz
Head, Patient Advocacy and Public Affairs

Questions & Answers:

Will you change the Zolgensma label, or recommendations around treatment?

Hepatoxicity, including transaminitis, acute liver injury, and acute liver failure, is currently included in the Warnings & Precautions section of the Zolgensma labeling information. As with all commercial products, we continually monitor the safety of Zolgensma. Pending health authority review and approval, the Zolgensma label will be updated to inform prescribers that fatal acute liver failure has been reported. Additionally, communications distributed to prescribers stress the importance of enhanced monitoring of liver function during the corticosteroid tapering period, and for at least three months after Zolgensma infusion, and/or at other times as clinically indicated.

How old were the patients, and when were they treated? Are there any other details you can provide?

To protect patient privacy, we can't discuss many details of any individual patients. What we can share is that the two fatal cases of acute liver failure occurred in Kazakhstan and Russia at approximately 6 to 7 weeks post Zolgensma infusion, and hepatotoxicity presented at approximately 1-10 days following the initiation of the corticosteroid taper. The ages of the patients were 4 months and 28 months; both of which fit the indication where they were treated.

Indication and Important Safety Information for ZOLGENSMA® (onasemnogene abeparvovec-xioi) suspension, for intravenous infusion

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 a vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

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

- ZOLGENSMA can increase liver enzyme levels and cause acute serious liver injury or acute liver failure.
- 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, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

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

- Infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see any signs of a possible 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 the patient experiences unexpected bleeding or bruising.
- Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

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.

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