Guidance for Appealing Denials

zolgensma®
(onasemnogene abeparvovec-xioi)
suspension for intravenous infusion

Spinal muscular atrophy (SMA) is a progressive disease characterized by irreversible motor neuron loss. Early treatment can help maximize clinical benefit and improve patient outcomes.

This guide provides best practices to craft an appeal if treatment with ZOLGENSMA® (onasemnogene abeparvovec-xioi) is denied by your patient's health plan. **The appeals process may vary by plan, but you may appeal by phone or letter, request a peer-to-peer review with an appropriate specialist after an initial denial, and escalate to an external review by a state or federal review board if the appeal is denied by the health plan. You may request a determination be made within 72 hours for claims involving urgent care.**

1 **Review the patient-specific denial letter and gather the necessary information to address the reason for denial**

2 **Package the necessary information for submission with the appeal. Information may vary based on the reason for denial, but may include**

- Patient-specific denial letter
- Health plan policy as published or communicated
- Patient's clinical chart data, including all lab test results, diagnosis confirmation, documentation of pulmonary and motor function, disease progression, nutritional status, and swallowing evaluation
  - Lab tests to identify appropriate patients include tests to confirm *SMN1* gene deletion or mutation, confirm *SMN2* copy numbers, and identify levels of anti-AAV9 antibodies
  - Patients denied for elevated anti-AAV9 antibody titers need to be retested until results show that antibody levels are in the acceptable range
- ZOLGENSMA product information and relevant supporting clinical literature

3 **Include the following key elements in your appeals call or letter of medical necessity**

- Confirm the reason for denial and be sure to ask clarifying questions as needed
- Reiterate the request for treatment. A letter of medical necessity can be used to better emphasize the need for treatment. Carefully highlight the key reasons for denial and address them with specific clinical rationale. Be as detailed as possible when addressing each concern stated in the denial letter
  - If patients were denied for:
    - Nonspecific *SMN2* copy numbers (eg, 4+ copies), then submit clarifying lab results showing the precise number of *SMN2* copies
    - Anti-AAV9 antibody titers, then submit the results of a follow-up test showing acceptable antibody levels
- Communicate the importance of treating early to prevent additional motor neuron loss. If relevant, describe the natural history of SMA
- Request a decision be made within 72 hours due to clinical urgency
- Escalate the appeal by requesting a peer-to-peer review with a specialist or an external review if you have already had a peer-to-peer review

4 **If appealing by letter, attach a copy of the denial letter to the appeal letter before sending. You may wish to include a list of supporting clinical literature you believe would be appropriate**

5 **For more information and resources regarding the appeals process and other access-related questions, visit www.zolgensmareimbursement.com**

Please contact the OneGene Program® at **855-441-GENE (4363), Monday-Friday (8 AM to 8 PM ET)**, for any plan-specific questions regarding the appeals process

AAV9, adeno-associated virus 9; *SMN1*, *survival motor neuron 1*; *SMN2*, *survival motor neuron 2*.

Please see Indication and Important Safety Information on the next page and the accompanying Full Prescribing Information, including Boxed Warning for Serious Liver Injury and Acute Liver Failure.

Indication and Important Safety Information

zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion

Indication

ZOLGENSMA is an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene.

Limitations of Use

The safety and effectiveness of repeat administration or the use in patients with advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence) has not been evaluated with ZOLGENSMA.

Important Safety Information

BOXED WARNING: Serious Liver Injury and Acute Liver Failure

Cases of acute liver failure with fatal outcomes have been reported. Acute serious liver injury, acute liver failure, and elevated aminotransferases can also occur with ZOLGENSMA. Patients with preexisting liver impairment may be at higher risk. Prior to infusion, assess liver function of all patients by clinical examination and laboratory testing. Administer systemic corticosteroid to all patients before and after ZOLGENSMA infusion. Continue to monitor liver function for at least 3 months after infusion, and at other times as clinically indicated. If acute serious liver injury or acute liver failure is suspected, promptly consult a pediatric gastroenterologist or hepatologist.

WARNINGS AND PRECAUTIONS

Systemic Immune Response

Patients with underlying active infection, either acute or chronic uncontrolled, could be at an increased risk of serious systemic immune response. Administer ZOLGENSMA to patients who are clinically stable in their overall health status (e.g., hydration and nutritional status, absence of infection). Postpone ZOLGENSMA in patients with infections until the infection has resolved and the patient is clinically stable.

Thrombocytopenia

Transient decreases in platelet counts, some of which met the criteria for thrombocytopenia, were typically observed within the first two weeks after ZOLGENSMA infusion. Monitor platelet counts before ZOLGENSMA infusion and on a regular basis for at least 3 months afterwards.

Thrombotic Microangiopathy

Cases of thrombotic microangiopathy (TMA) were reported to occur generally within the first two weeks after ZOLGENSMA infusion. TMA can result in life-threatening or fatal outcomes. Obtain baseline creatinine and complete blood count before ZOLGENSMA infusion. Following infusion, monitor platelet counts closely as well as other signs and symptoms of TMA. Consult a pediatric hematologist and/or pediatric nephrologist immediately to manage as clinically indicated.

Elevated Troponin-I

Increases in cardiac troponin-I levels were observed following ZOLGENSMA infusion. Monitor troponin-I before ZOLGENSMA infusion and on a regular basis for at least 3 months afterwards. Consider consultation with a cardiologist if troponin elevations are accompanied by clinical signs or symptoms.

AAV Vector Integration and Risk of Tumorigenicity

There is a theoretical risk of tumorigenicity due to integration of AAV vector DNA into the genome. Cases of tumor have been reported in patients who received ZOLGENSMA post-approval; information on the cases is limited and causal relationship cannot be established. Report cases of tumor development in patients who received ZOLGENSMA to Novartis Gene Therapies, Inc. at 1-833-828-3947.

ADVERSE REACTIONS

The most commonly observed adverse reactions (incidence ≥5%) in clinical studies were elevated aminotransferases and vomiting.

Please see accompanying Full Prescribing Information.

Reference: Glascock J, Sampson J, Haidet-Phillips A, et al. Treatment algorithm for infants diagnosed with spinal muscular atrophy through newborn screening. *J Neuromuscul Dis*. 2018;5(2):145-158. doi:10.3233/JND-180304.

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