Zolgensma (onasemnogene abeparvovec-xioi)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Zolgensma
- **Generic name:** Onasemnogene abeparvovec-xioi
- **Pharmacological class:** Adeno-associated virus vector-based gene therapy
- **Strength and Formulation:** 2.0×10^{13} vector genomes (vg); per mL; susp for IV infusion; preservative-free
- **Manufacturer:** AveXis
- **How supplied:** Customized kit—1 (2–9 vials + alcohol wipes)
- **Legal Classification:** Rx

Zolgensma


onasemnogene abeparvovec-xioi
ZOLGENSMA
Rx ONLY
Suspension for intravenous infusion.
ZOLGENSMA is a registered trademark of AveXis, Inc.
Manufactured by AveXis, Inc.
Bannockburn, IL 60015
©2019 AveXis, Inc.
US License No: 2104 1729
onasemnogene abeparvovec-xioi
ZOLGENSMA
Rx ONLY
Suspension for intravenous infusion.
2.0 x 10^13 vector genomes/mL
See enclosed prescribing information for dosage and directions for use.
Contains no preservatives.
Discard any unused portion.
Upon receipt store refrigerated at 2°C to 8°C (36°F to 46°F).
Must use within 14 days of receipt.
Store in the original carton until time of use.
DO NOT SHAKE | DO NOT REFREEZE
ZOLGENSMA is a registered trademark of AveXis, Inc.
Manufactured by AveXis, Inc.
Bannockburn, IL 60015
©2019 AveXis, Inc. 1729
5.5 mL
1672
NDC 71894-115-01
onasemnogene ab
ZOLGENSMA
Rx ONLY
Suspension for intravenous infusion.
See enclosed prescribing information for dosage and directions for use.
Manufactured by AveXis, Inc.
Bannockburn, IL 60015
US License No: 2104

Indication

- Treatment of pediatrics <2yrs of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene

Dosage & Administration

- **≥2yrs: not applicable**
- Give as a slow IV infusion over 60mins
  <2yrs: 1.1×10^{14} vector genomes (vg)/kg (see full labeling)
- Starting one day prior to Zolgensma infusion: **give systemic corticosteroids** equivalent to oral prednisolone 1mg/kg/day for 30 days, then taper dose for the next 28 days if LFTs are unremarkable

Considerations for Special Populations

- **Pediatric:** administration to premature neonates before reaching full-term gestational age is not recommended, because concomitant treatment with corticosteroids may adversely affect neurological development; delay infusion until the corresponding full-term gestational age is reached
  - Safety studied in patients 0.3 to 7.9 months (weight range 3kg to 8.4kg)
  - Efficacy studied in patients 0.5 to 7.9 months (weight range 3.6kg to 8.4kg)
- **Hepatic impairment:** elevation of aminotransferases was observed in clinical trials

Boxed Warning

- Acute **serious liver injury** and elevated aminotransferases can occur

Warnings/Precautions

- Risk of acute serious liver injury
- **Monitor liver function** prior to infusion, weekly for the 1st month, then every other week for the 2nd/3rd months until unremarkable results
- **Monitor platelets, troponin-I** prior to infusion, weekly for the 1st month, then every other week (platelets) and monthly (troponin-I) for the 2nd/3rd months until levels return to baseline
- Perform **baseline anti-AAV9 antibody testing** prior to infusion; may retest if titers are >1:50

Interactions

- **Adjust vaccination schedule** to accommodate concomitant corticosteroid use before and after infusion

Adverse Reactions

- **Most common** (≥5%): elevated aminotransferases, vomiting
- **Others**: thrombocytopenia, elevated troponin-I

Mechanism of Action

- Zolgensma is a **recombinant AAV9-based gene therapy** designed to deliver a copy of the gene encoding the human SMN protein
- SMA is caused by a bi-allelic mutation in the *SMN1* gene, which results in insufficient SMN protein expression
- Intravenous administration of Zolgensma that results in cell transduction and expression of the SMN protein has been observed in 2 human case studies

Clinical Studies

- Approval was based on data from the ongoing phase 3 **STR1VE trial** and the completed phase 1 **START trial**
- In both studies, patients were administered a single-dose intravenous infusion of Zolgensma
- Efficacy was established on the basis of survival, and achievement of developmental motor milestones (ie, sitting without support)

Clinical Studies

- **Survival** was defined as time from birth to either death or permanent ventilation
- **Permanent ventilation** was defined as requiring invasive ventilation (tracheostomy), or respiratory assistance for ≥16 hours per day (including noninvasive ventilatory support) continuously for ≥14 days in the absence of an acute reversible illness, excluding perioperative ventilation
- Efficacy was also supported by assessments of ventilator use, nutritional support and scores on the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)

Clinical Studies

- The **ongoing clinical trial** enrolled 21 patients (10 male and 11 female) with infantile-onset SMA

- By data cutoff, results showed 13 of the 19 patients reached 14 months of age without permanent ventilation; 10 of the 21 patients (47.6%) achieved the ability to sit without support for ≥30 seconds between 9.2 and 16.9 months of age (mean age was 12.1 months); 16 of the 19 patients had not required daily non-invasive ventilator (NIV) use

Clinical Studies

- The **completed clinical trial** enrolled 15 patients (6 male and 9 female) with infantile-onset SMA, 3 in a low-dose cohort and 12 in a high-dose cohort

- By 24 months following infusion, 1 patient in the low-dose cohort met the endpoint of permanent ventilation; all 12 patients in the high-dose cohort were alive without permanent ventilation

- None of the patients in the low-dose cohort were able to sit without support, or to stand or walk; in the high-dose cohort, 9 of the 12 patients (75.0%) were able to sit without support for ≥30 seconds, and 2 patients (16.7%) were able to stand and walk without assistance

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/zolgensma/