PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Zolgensma®
Suspension for intravenous infusion

Composition

Active ingredient: onasemnogene abeparvovec

Each vial contains: 2.0×10^{13} vector genomes/mL

Inactive and allergenic ingredients: see section 2 "Important information about some of the ingredients in this medicine" and section 6 "Further information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed as treatment for your child.

Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

In addition to the leaflet, Zolgensma has a Patient Safety Information Card – Parent Guidance Leaflet. This card contains important safety information which you must know before starting and during the course of treatment with Zolgensma and follow. Read the Patient Safety Information Card and patient leaflet before starting to use the preparation. Keep the card for further reference, when needed.

Warning: Serious acute liver injury, acute liver failure or elevated liver enzymes.

The medicine may cause an increase in liver enzyme levels, serious liver injury or acute liver failure. Cases of acute liver failure with fatal outcomes have been reported.

Patients with preexisting impaired liver function may be at increased risk.

Before injecting the medicine, a liver function test should be performed.

For this reason, the patient should be given an oral steroid medicine starting the day before Zolgensma treatment, and for at least another 30 days after administration of the one-time treatment. After the treatment, the patient will undergo a series of routine blood tests to monitor the liver function. The liver function should be monitored for at least 3 months after administration of treatment, and at other times as clinically indicated.

1. WHAT IS THE MEDICINE INTENDED FOR?

Zolgensma is intended for the treatment of:

- patients with 5q spinal muscular atrophy (SMA) with a biallelic mutation in the SMN1 gene and a clinical diagnosis of spinal muscular atrophy type 1 (SMA type 1) or
- patients with 5q spinal muscular atrophy (SMA) with a biallelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.

Therapeutic group: Gene therapy

How the medicine works:

SMA is a disease that occurs when there is an abnormal or missing version of a gene, which is needed to make an essential protein called Survival Motor Neuron (SMN) protein. Lack of SMN protein causes nerves that control muscles (motor neurons) to die. This results in muscles becoming weak and wasting away, with eventual loss of movement.

This medicine works by supplying a functioning copy of the SMN1 gene which helps the body produce enough SMN protein. The gene is delivered into the cells where it is needed using a virus carrier that does not cause disease in humans.

2. BEFORE USING THE MEDICINE

Do not use the medicine if

Your child is sensitive (allergic) to the active ingredient (onasemnogene abeparvovec) or to any of the additional ingredients contained in the medicine (as listed in section 6).

Special warnings regarding use of the medicine

Liver problems

Before treatment with Zolgensma, tell the doctor if your child has had any liver problems. This medicine can lead to an increase in enzymes (proteins found within the body) produced by the liver or injury to the liver. Injury to the liver can lead to serious outcomes, including liver failure and death. Possible signs you need to look out for after giving this medicine to your child include vomiting, jaundice (yellowing of the skin or the whites of the eyes), or reduced alertness (see section 4 for more information). Tell the attending doctor immediately if you notice that your child is developing any symptoms suggestive of injury to the liver.

Infection

An infection (e.g., cold, flu, bronchiolitis) before or after Zolgensma treatment may lead to serious complications. Caregivers and close contacts with the patient should follow infection prevention practices (e.g., hand hygiene, coughing/sneezing etiquette, limiting potential contacts). Look out for possible signs of an infection, such as coughing, wheezing, sneezing, runny nose, sore throat or fever. Tell the attending doctor immediately if you notice that your child is developing any symptoms suggestive of infection **before** or **after** Zolgensma treatment.

Abnormal clotting of blood in small blood vessels (thrombotic microangiopathy)

There have been reports of patients who developed thrombotic microangiopathy generally within two weeks after Zolgensma treatment. Thrombotic microangiopathy is accompanied by a decrease in red blood cells and cells involved in blood clotting (platelets) and can be fatal. These blood clots could affect your child's kidneys. Your child's doctor may want to check your child's blood (platelet counts) and blood pressure. Possible signs you need to look out for after Zolgensma is given to your child include bruising easily, seizures (fits) or decrease in urine output (see section 4 for more information). Seek urgent medical attention if your child develops any of these signs.

Blood, organ, tissue and cell donation

After your child has been treated with Zolgensma, he will not be able to donate blood, organs, tissues or cells. This is because Zolgensma is a gene therapy.

Children and adolescents

The safety and efficacy of onasemnogene abeparvovec in premature infants before reaching full gestational age, have not been proven. No data is available. Administration of onasemnogene abeparvovec should be considered with caution as concomitant treatment with corticosteroids may adversely affect neurological development.

There is limited experience in patients 2 years of age or older or patients with a body weight over 13.5 kg. The safety and efficacy of onasemnogene abeparvovec in these patients have not been established.

Tests and follow-up

Before treatment, the doctor will perform an antibody test (AAV9 antibodies). The test will help decide if the medicine is suitable for your child.

Zolgensma may lead to an increase in liver enzymes or injury to the liver.

Before starting treatment with Zolgensma, your child will undergo a blood test to check liver function. Your child will also undergo routine blood tests at least 3 months after treatment to monitor for an increase in liver enzymes.

Zolgensma may lower blood platelet counts (thrombocytopenia).

Look out for possible signs of a low blood platelet count after your child is given Zolgensma, such as abnormal bruising or bleeding (see section 4 for more information). Most of the reported cases of a low blood platelet count occurred within the first two weeks after the child was given Zolgensma.

Zolgensma can raise levels of a heart protein called troponin-I that may indicate injury to the heart.

Look out for possible signs of heart problems after your child is given Zolgensma, such as pale grey or blue skin colour, difficulty in breathing, swelling of the arms and legs or of the stomach (see section 4 for more information).

Before starting treatment with Zolgensma, your child will have blood tests to check the amount of blood cells (including red blood cells and platelets), as well as troponin-I level in the body.

Your child will also have blood tests to check creatinine level, which is an indicator of kidney function.

Your child will also have regular blood tests for a period of time after treatment to monitor for changes in platelet and troponin-I levels.

Drug interactions

If your child is taking, or has recently taken, other medicines, including non-prescription medicines or nutritional supplements, tell the doctor, nurse or pharmacist.

Prednisolone

Your child will also be treated with corticosteroids such as prednisolone for about two months or longer (see also section 3) as part of Zolgensma treatment. The corticosteroid treatment will help manage any increase in liver enzymes that your child could develop after being given Zolgensma.

Vaccinations

As corticosteroids can affect the body's immune (defense) system, **the doctor may decide to delay giving vaccinations** while your child is receiving corticosteroid treatment. Talk to the doctor or nurse if you have any questions.

Pregnancy, breastfeeding and fertility

There is no information regarding use of the preparation in pregnant or breastfeeding women. No studies have been performed to assess the effect of the preparation on patient fertility.

Driving and operating machinery

The medicine has no or a negligible effect on ability to drive or operate machinery.

Important information about some of the ingredients of the medicine

Zolgensma contains 4.6 mg sodium in each mL of medicine. This amount is 0.23% of the maximum dose recommended for an adult by the World Health Organization (WHO), which is 2 grams of sodium. Each 5.5 mL vial contains 25.3 mg sodium, and each 8.3 mL vial contains 38.2 mg sodium.

Additional information for parents/caregiver

Advanced SMA

Zolgensma can rescue living motor neurons, but does not rescue dead motor neurons. Children with less severe symptoms of SMA (such as absent reflexes or reduced muscle tone) may have sufficient living motor neurons to benefit significantly from Zolgensma treatment. Zolgensma may not work as well in children with severe muscle weakness or paralysis, breathing problems or who are unable to swallow, or in children who have significant malformations (such as heart defects), including patients with SMA Type 0, as there may be limited potential improvement after treatment with Zolgensma. Your child's doctor will decide if your child should be given this medicine.

Hygiene care

The active ingredient in Zolgensma may temporarily be excreted through your child's bodily waste and fluids. Parents and caregivers should follow good hand hygiene for up to 1 month after giving Zolgensma to the child. Wear protective gloves when coming into direct contact with the child's bodily fluids or waste and wash hands thoroughly afterwards with soap and warm running water, or an alcohol-based hand sanitiser. Double bags should be used to dispose of soiled nappies and other waste. Nappies may still be disposed of in the household waste. You should continue to follow these instructions for at least one month after your child's treatment with Zolgensma. Talk to your child's doctor or nurse if you have any questions.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the medicine according to the doctor's instructions. **The dosage and the treatment regimen will be determined by the doctor only.**

Zolgensma injection will be given to your child by a doctor or nurse trained in treatment of your child's medical condition.

The doctor will determine the amount of medicine your child will receive according to your child's weight.

The dose will be given by **a single** intravenous injection that will take approximately one hour.

Zolgensma will be given to your child once only.

Your child will also be given prednisolone (or another corticosteroid) by mouth, starting 24 hours before being given Zolgensma. The dosage of corticosteroid will also depend on your child's weight. The doctor will work out the total dosage to give.

Your child will be given corticosteroid treatment daily for about two months after the Zolgensma treatment, or until your child's liver enzymes decrease to an acceptable level. The doctor will slowly reduce the dosage of corticosteroids until treatment can be fully stopped.

Do not exceed the recommended dosage.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Zolgensma may cause side effects in some users. Do not be alarmed by reading the list of side effects. Your child may not suffer from any of them.

Seek urgent medical attention if your child develops any of the following serious side effects:

Common side effects – occur in 1-10 in 100 users:

- bruising or bleeding for longer than usual when your child gets hurt – these may be signs of a low blood platelet count
- pale grey or blue skin colour, difficulty in breathing (e.g., rapid breathing, shortness of breath), swelling of the arms and legs or of the stomach – these may be signs of possible problems with the heart

Unknown frequency (frequency cannot be estimated from the available data):

- vomiting, jaundice (yellowing of the skin or of the whites of the eyes) or reduced alertness – these may be signs of injury to the liver (including liver failure)
- bruising easily, seizures, decrease in urine output – these may be signs of thrombotic microangiopathy.

Additional side effects

Tell the doctor or nurse if your child develops the following side effects:

Very common side effects – effects that occur in more than one in ten users:

- increases in liver enzymes seen in blood tests

Common side effects – occur in 1-10 in 100 users:

- vomiting
- fever
- thrombocytopenia (low platelet level)
- increased troponin protein level

If a side effect occurs, if one of the side effects worsens, or if you suffer from side effects not mentioned in the leaflet, consult the doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

The following information is intended for healthcare professionals who will prepare and give the treatment.

Storage conditions:

Do not use this medicine after the expiry date (exp. date) which appears on the bottle and carton. The expiry date refers to the last day of that month.

Vials will be transported frozen (-60°C).

Immediately upon receipt of the medicine from the distributor, store in a refrigerator, at a temperature of 2-8°C, in the original package.

Use the medicine within 14 days of receiving delivery of the medicine.

Do not refreeze the medicine. Do not shake.

This medicine contains genetically-modified organisms. Unused medicine or waste material must be disposed of in compliance with the local guidelines on handling of biological waste. As this medicine will be given by a doctor, the doctor is responsible for the correct disposal of the product. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Sodium chloride, tromethamine, magnesium chloride, poloxamer 188, hydrochloric acid, water for injection

What the medicine looks like and the content of the package:

Zolgensma is a clear to slightly opaque, colourless to faint white solution for infusion.

Zolgensma is supplied in vials containing a nominal fill volume of either 5.5 mL or 8.3 mL. Each vial is for single use only.

Each carton will contain between 2 and 14 vials.

Registration Holder and Importer and its address:

Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 165 75 36125

Revised in April 2023 according to MOH guidelines.

ZOL APL APR23 V3

המידע הבא מיועד לצוות רפואי בלבד:

The following information is intended for healthcare professionals only:

المعلومات التالية مخصصة للطاقم الطبي فقط:

Important: Please refer to the Summary of Product Characteristics (SmPC) before using.

Each vial is for single use only.

This medicinal product contains genetically-modified organisms. Local guidelines on handling of biological waste should be followed.

Handling

- Zolgensma should be handled aseptically under sterile conditions.
- Personal protective equipment (including gloves, safety goggles, laboratory coat and sleeves) should be worn while handling or administering Zolgensma. Personnel should not work with Zolgensma if skin is cut or scratched.
- All spills of Zolgensma must be wiped with absorbent gauze pads and the spill area must be disinfected using a bleach solution followed by alcohol wipes. All clean-up materials must be double bagged and disposed of in accordance with the local guidelines on handling of biological waste.
- All materials that may have come in contact with Zolgensma (e.g., vial, all materials used for injection, including sterile drapes and needles) must be disposed of in accordance with the local guidelines on handling of biological waste.

Accidental exposure

Accidental exposure to Zolgensma must be avoided.

In case of accidental exposure to skin, the affected area must be thoroughly cleansed with soap and water for at least 15 minutes. In case of accidental exposure to eyes, the affected area must be thoroughly flushed with water for at least 15 minutes.

Storage

Vials will be transported frozen (at or below -60°C). Upon receipt, vials should be refrigerated at 2°C to 8°C immediately, and in the original carton. Zolgensma therapy should be initiated within 14 days of receipt of vials. The date of receipt should be marked on the original carton before the product is stored in the refrigerator.

Preparation

Vials should be thawed before use:

- For packs containing up to 9 vials – thaw for approximately 12 hours in the refrigerator (2°C to 8°C) or 4 hours at room temperature (20°C to 25°C).
- For packs containing up to 14 vials – thaw for approximately 16 hours in the refrigerator (2°C to 8°C) or 6 hours at room temperature (20°C to 25°C).

Do not use Zolgensma unless thawed.

Once thawed, the medicinal product should not be re-frozen.

After thawing, gently swirl Zolgensma. Do NOT shake.

Do not use this medicine if you notice any particles or discolouration once the frozen product has thawed and prior to administration.

After thawing, Zolgensma should be given as soon as possible.

Administration

Zolgensma should be given to patients ONCE only.

The dose of Zolgensma and exact number of vials required for each patient is calculated according to the patient's weight (see SmPC sections 4.2 and 6.5).

To administer Zolgensma, draw the entire dose volume into the syringe. Once the dose volume is drawn into the syringe, it must be administered within 8 hours. Remove any air in the syringe before administering to the patient via intravenous infusion through a venous catheter. Insertion of a secondary ('back-up') catheter is recommended in case of blockage in the primary catheter.

Zolgensma should be administered with the syringe pump as a single intravenous infusion with a slow infusion of approximately 60 minutes. It should be administered as an intravenous infusion only. It should not be administered as a rapid intravenous injection or bolus. Following completion of infusion, the line should be flushed with sodium chloride 9 mg/mL (0.9%) solution for injection.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with the local guidelines on handling of biological waste.

Temporary Zolgensma shedding may occur, primarily through bodily waste. Caregivers and patients' families should be advised on the following instructions for the proper handling of patients' bodily fluids and waste:

- Good hand hygiene (wearing protective gloves and washing hands thoroughly afterwards with soap and warm running water, or an alcohol-based hand sanitiser) is required when coming into direct contact with patient's bodily fluids and waste for a minimum of 1 month after Zolgensma treatment.
- Disposable nappies should be sealed in double plastic bags and can be disposed of in household waste.