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} vg/mL

For the list of inactive ingredients, see 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 and follow before starting and during the course of treatment with Zolgensma. Read the Patient Safety Information Card and patient leaflet before starting to use the preparation. Keep the card for reference, when needed.

Warning: Acute serious liver injury, acute liver failure or elevated liver enzymes.

This 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 pre-existing impaired liver function may be at higher risk.

Before injecting the medicine, perform a liver function test.

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

1. WHAT IS THE MEDICINE INTENDED FOR?

Zolgensma is a genetic treatment that contains a viral vector intended to treat children up to two years of age, diagnosed with SMA (spinal muscular atrophy) with a mutation in the **SMN1** gene.

Therapeutic group: Gene therapy preparations.

How the medicine works:

SMA arises from a defect in a gene called SMN1. The defect in this gene leads to inadequate production of a protein called SMN. Zolgensma is a genetic therapy that contains a viral vector that transfers the gene encoding the missing protein. After administering Zolgensma, the body can correctly produce adequate amounts of the missing protein.

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

Acute serious liver injury

This medicine may cause an increase in liver enzyme levels, serious liver injury or acute liver failure, which can result in life-threatening or fatal outcomes. Patients with pre-existing impaired liver function may be at higher risk.

Before injecting the medicine, perform a liver function test.

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

Inform the attending doctor in cases of yellowish skin or eye color, when the patient misses or vomits the steroid dose or if the patient experiences a decrease in alertness.

Infectious diseases (e.g., common cold, influenza, bronchiolitis, otitis media [middle ear infection], gastroenteritis [stomach flu]) before or after treatment with Zolgensma may lead to serious complications. Pay attention to the possible signs of these ailments, such as cough, wheezing, sneezing, runny nose, sore throat or fever. Inform the attending doctor immediately in cases of onset of symptoms indicative of a possible infection.

Thrombocytopenia – low platelet level

Zolgensma may lead to decreased platelet counts and to cause an increased risk of bruises and bleeding. Perform a platelet count every week during the first month after treatment, and then every two weeks during the second and third months, until platelet levels return to normal.

Inform the attending doctor of cases of bruising ("black and blue marks") or bleeding.

Thrombotic microangiopathy (TMA)

Inform the parents and caregivers that Zolgensma may lower platelet levels as well as red blood cell counts, may cause acute kidney damage, and increase the risk of bleeding and bruising, these symptoms may be indicative of TMA.

Inform the parents and caregivers that TMA is a phenomenon reported under Zolgensma treatment, and may occur about a week after Zolgensma infusion. Inform the parents and caregivers to refer to the attending doctor immediately if unexpected bruising or bleeding, convulsion, or decreased urination occurs following Zolgensma treatment.

Troponin-I levels (a protein related to heart activity)

There may be an increase in blood levels of this protein. Therefore, a test for levels of this protein will be performed every week in the first month after the treatment and then once a month in the second and third months, until the levels return to normal.

Treating bodily secretions

Zolgensma is primarily cleared from the body through patient secretions.

Therefore, for approximately one month after the infusion, diapers with stools should be placed in two plastic bags and thrown into a regular waste bin. In addition, be careful to wash your hands after contact with stools, secretions and bodily fluids.

Administration to premature babies

Administration of Zolgensma to premature infants before reaching full-term gestational age is not recommended, as the required ancillary steroid treatment may have a detrimental effect on their neurological development.

Tests and follow up

Before and after administering the Zolgensma infusion, the doctor will refer your child for tests:

- Liver function (see details in Warning section above).
- Platelet and troponin-I count (see details in Warning section above).
- Presence of anti-AAV9 antibodies.

Drug interactions

Consult the doctor regarding vaccination times before and after administration of the medicine, especially the MMR (measles, mumps, rubella), varicella (chicken pox) and seasonal prophylactic RSV (respiratory syncytial virus) vaccine.

Pregnancy, breastfeeding and fertility

There is no information regarding use of the preparation in pregnant women. There is no information about use in breastfeeding women and on the presence of the preparation in breast milk, and what its effect is on babies. No studies have been performed to assess the effect of the preparation on patient fertility.

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 by the World Health Organization (WHO) for an adult, which is 2 gram sodium. Each 5.5 mL vial contains 25.3 mg sodium and each 8.3 mL vial contains 38.2 mg sodium.

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 will be injected to your child by a doctor or nurse experienced in treatment of your child's medical condition.

The amount of Zolgensma your child will receive will be calculated by your child's doctor according to your child's weight. The dose is calculated in units called vector genomes. The recommended dosage is: 1.1×10^{14} vector genomes per kilogram body weight.

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

Do not exceed the recommended dose.

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.

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

Increased liver enzymes and vomiting.

Post marketing side effects reported (unknown frequency)

Acute liver failure (including fatal cases), acute liver injury, fever, increased troponin protein level, thrombocytopenia (low platelet level), thrombotic microangiopathy.

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.

Storage conditions: The medicine is delivered frozen. Immediately after receiving the medicine from the distributor, store it in a refrigerator, at a temperature of 2°C-8°C. Zolgensma is stable for 14 days when stored in a refrigerator. Do not refreeze the medicine. Use within 14 days of receiving the delivery of the medicine.

Do not shake. Store in the original package until use.

6. FURTHER INFORMATION

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

Water for Injection, Sodium Chloride, Tromethamine, Magnesium Chloride, Poloxamer 188, Hydrochloric Acid.

What the medicine looks like and the contents of the package: The medicine contains a kit with 2-9 vials.

Registration Holder and Importer: 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 September 2022 according to MOH guidelines.