PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrZOLGENSMA®

onasemnogene abeparvovec

Read this carefully before your child receives **Zolgensma®**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your child's medical condition and treatment and ask if there is any new information about **Zolgensma**.

What is Zolgensma used for?

Zolgensma is a type of medicine called a 'gene therapy'. It contains the active ingredient onasemnogene abeparvovec, which contains human genetic material.

Zolgensma is used to treat babies and young children who have a rare, serious inherited condition called 'spinal muscular atrophy' (SMA).

How does Zolgensma work?

Zolgensma supplies a fully functioning copy of the survival motor neuron 1 (SMN1) gene, which helps cells produce SMN protein necessary for the survival of nerves that control muscles (motor neurons). Patients treated with Zolgensma showed improvements relative to the usual progress of SMA. These improvements included the avoidance of death or permanent need for breathing help, and achievement of developmental motor milestones (e.g., head control, sitting, and standing).

What are the ingredients in Zolgensma?

Medicinal ingredient: onasemnogene abeparvovec.

Non-medicinal ingredients: hydrochloric acid (for pH adjustment), magnesium chloride, poloxamer 188, sodium chloride, tromethamine, and water for injection.

Zolgensma comes in the following dosage forms:

Zolgensma is a clear to slightly cloudy solution for infusion. Each vial of Zolgensma contains onasemnogene abeparvovec at a nominal concentration of 2×10^{13} vg/mL.

Do not use Zolgensma if:

Your child is allergic to onasemnogene abeparvovec or any of the other ingredients of this medicine listed in this leaflet.

To help avoid side effects and ensure proper use, talk to your healthcare professional before your child is given Zolgensma. Talk about any health conditions or problems your child may have.

Warnings you should know about:

Your child's healthcare professional will test your child's blood for antibodies against part of this medicine to help decide if this medicine is suitable for your child.

Liver problems

If your child has had any problems with his/her liver, talk to your child's healthcare professional before your child is treated with this medicine. Zolgensma can cause an immune response that could damage 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 your child is given this medicine include vomiting, jaundice (yellowing of the skin or of the whites of the eyes) or reduced alertness (see **What are possible side effects from using Zolgensma?** for more information). Tell your child's healthcare professional immediately if you notice your child develops any symptoms suggestive of injury to the liver. Your child will have a blood test to check liver function before starting treatment with Zolgensma. He/she will also have regular blood tests for at least 3 months after being treated with Zolgensma to check for increases in liver enzymes.

Educational materials for caregivers related to the risks of liver problems are available through the manufacturer.

Infections

If your child develops an infection (such as cold, flu, or bronchiolitis) before or after being treated with Zolgensma, this could lead to more serious problems, which could be life-threatening. Caregivers and close contacts with the patient should follow infection prevention practices (e.g., hand hygiene, respiratory/cough etiquette, limit potential contacts). Signs of a possible infection that you need to check for in your child include coughing, wheezing, sneezing, runny nose, sore throat, or fever. Tell your child's healthcare professional immediately if you notice that your child develops any signs suggestive of infection **before** or **after** Zolgensma treatment.

Risk of bleeding and blood clotting problems

Zolgensma can lower the number of a certain type of cell in the blood, called blood-platelets (a condition called thrombocytopenia). This has been observed to generally occur within the first two weeks after Zolgensma treatment. Possible signs of a low blood-platelet count you need to check for after your child is treated with Zolgensma include abnormal bruising, blood in urine or feces, or nosebleeds (see **What are possible side effects from using Zolgensma?** for more information).

Blood clotting problems in small blood vessels (a serious and potentially life-threatening condition called thrombotic microangiopathy) have been reported in some patients usually within the first two weeks after treatment with Zolgensma. This happened at the same time as a decrease in red blood cells and a decrease in cells involved in clotting (blood-platelets). These blood clots could damage your child's kidneys. Before starting treatment with Zolgensma, your child will have a blood test to check the amount of blood cells (including red blood cells and platelets) as well as creatinine level, which is an indicator of how the kidneys are working. Following Zolgensma treatment, your child's healthcare professional may want to check your child's blood cells (platelet counts) and blood pressure. Seek urgent medical attention if your child starts to bruise easily, has seizures (fits), develops a fever, or passes less urine than usual after Zolgensma treatment (see **What are possible side effects from using Zolgensma?** for more information).

Educational materials for caregivers related to the risks of thrombocytopenia and thrombotic microangiopathy are available through the manufacturer.

Heart problems

Zolgensma may cause raised levels in the blood of a protein specific to the heart called 'troponin-I'. Increased levels may indicate damage to the heart. Possible signs you need to look out for after your child is given Zolgensma include pale grey/blue skin colour, difficulty in breathing, and swelling of the arm/legs or abdomen (see **What are possible side effects from using Zolgensma?** for more information).

Risk of tumours associated with potential insertion of gene therapy DNA into the patient's DNA

There is a possibility that DNA from gene therapies such as Zolgensma can insert into the DNA of human body cells. As a consequence, Zolgensma could contribute to a risk of tumours. You should discuss this with your child's doctor. In the event of a tumour, your child's doctor may take a sample for further evaluation.

Additional information for parents/caregiver

Regular blood tests

Your child will have a blood test to check liver function before starting treatment with Zolgensma. He/she will also have regular blood tests for at least 3 months after being treated with Zolgensma to check for increases in liver enzymes.

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 creatinine and troponin-I levels. Your child will also have regular blood tests for at least three months after treatment with Zolgensma to check for possible changes in blood-platelets and troponin-I levels.

Advanced SMA

Zolgensma can save 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 enough live motor neurons to receive meaningful benefit from Zolgensma. Zolgensma may not work as well in children with severe muscle weakness or paralysis, with breathing problems, who are unable to swallow, or with critical malformation (such as heart defects). These signs suggest less potential for improvement from treatment with Zolgensma. Your child's healthcare professional will decide if your child should be treated with Zolgensma.

Hygiene care

The active substance in Zolgensma will be passed from your child's body in their waste. As parents/caregivers, you must follow additional hygiene practices for at least one month after your child is treated with Zolgensma. Wear protective gloves when coming into direct contact with your child's bodily fluids or waste and wash hands thoroughly afterward with soap and warm running water, or an alcohol-based hand sanitizer. Double bags should be used to dispose of soiled diapers and other waste. Disposable diapers may still be disposed of in household waste. Reusable diapers should not be used during the first month after Zolgensma treatment.

Talk to your child's doctor or nurse if you have any questions.

Tell your child's healthcare professional about all the medicines your child is taking, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

At this time, there are no known medicines that interact with Zolgensma.

Prednisolone

Your child will also be treated with a medicine called 'prednisolone' (see **How Zolgensma is given**) before and after his/her treatment with Zolgensma. Prednisolone is a type of medicine called a 'corticosteroid' which will help manage any potential liver damage that your child could develop after Zolgensma treatment. Your child's healthcare professional will decide if your child should be treated with prednisolone or a different corticosteroid.

Vaccinations

As corticosteroids can affect the body's immune system, **your child's healthcare professional may decide to delay giving some vaccinations** to your child while he/she is treated with prednisolone/corticosteroid. Talk to your child's healthcare professional if you have any questions.

How Zolgensma is given:

Zolgensma is given to your child by a healthcare professional trained in the delivery of gene therapy and in the management of SMA.

Zolgensma is given intravenously (into a vein) to your child by a single infusion (drip) over a period of 1 hour.

Usual dose:

The amount of Zolgensma your child will be given will be calculated based on their weight. The dose is measured in units called vector genomes.

The recommended dose is 1.1×10^{14} vector genomes per kilogram (kg) of body weight.

Zolgensma will be given to your child ONCE only.

Starting 24 hours before treated with Zolgensma, your child will also be given treatment with prednisolone (or another corticosteroid) by mouth. The dose of prednisolone will depend on your child's weight. The recommended dose of prednisolone is 1 mg per kg body weight daily. Your child's healthcare professional will calculate the correct total dose.

After treatment with Zolgensma, your child will be treated with prednisolone every day for approximately 2 months until your child's increased liver enzymes decrease to an acceptable level. Your child's dose of prednisolone will be slowly reduced until treatment can be fully stopped. **The prednisolone treatment must not be stopped suddenly.** Your child's healthcare professional will explain when and how they will stop this treatment for your child.

If you have any further questions on the use of Zolgensma or prednisolone, ask your child's healthcare professional.

Overdose:

There is no experience of overdose with Zolgensma.

If you think your child has been given too much Zolgensma, contact your child's healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If your child is unable to be treated with Zolgensma as planned, talk to your healthcare professional to ensure that Zolgensma can be given as soon as possible.

What are possible side effects from using Zolgensma?

Like all medicines, Zolgensma can cause side effects, although not everybody gets them.

Talk to your child's doctor or nurse if your child develops any side effects. These can include:

Very common (may affect more than 1 in 10 people)

- increases in liver enzymes (aminotransferases) seen in blood tests
- fever

Common (may affect up to 1 in 10 people):

- vomiting
- decreases in blood-platelets, seen in blood tests

These are not all the possible side effects your child may feel when taking Zolgensma. If your child experiences any side effects not listed here, contact your child's healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Bruising or bleeding for longer than usual if your child has been hurt, blood in urine or feces, nosebleeds (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 arm/legs or abdomen (signs of possible problems with the heart).			√
FREQUENCY NOT KNOWN			
Bruising easily, seizures (fits), decrease in urine output (signs of thrombotic microangiopathy).			√
Vomiting, yellowish skin or eyes, irritability/fussiness, swollen abdomen, sleeping more than normal (signs of liver injury/failure).			√

If your child has a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with their daily activities, talk to your child's healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Zolgensma will be managed and stored by healthcare professionals. Below are some of the guidelines for storing Zolgensma:

- 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.
- Do not use this medicine after the expiry date which is stated on the vial label and carton after EXP. The expiry date refers to the last day of that month.
- Keep out of reach and sight of children.

If you want more information about Zolgensma:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.novartis.ca, or by calling 1-800-363-8883.

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