ITVISMA TREATMENT GUIDE

itvisma®
(onasemnogene abeparvovec-brve)
suspension for intrathecal injection

Scarlette R., 17 years old
Student
Living with SMA
Scarlette hasn't received ITVISMA. She was compensated for her time.

For US Health Care Professionals only.

Instructions on how to administer ITVISMA to your patient

ITVISMA is the only one-time gene replacement therapy for patients aged 2 years and older—including children, teens, and adults—with spinal muscular atrophy (SMA).[1]

INDICATION

ITVISMA is indicated for the treatment of spinal muscular atrophy (SMA) in adult and pediatric patients 2 years of age and older with confirmed mutation in *survival motor neuron 1* (*SMN1*) gene.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: Serious Liver Injury

Acute serious liver injury can occur with ITVISMA. Hepatotoxicity, with elevated alanine transaminase (ALT) and/or aspartate transaminase (AST) levels, has occurred with ITVISMA. Patients with preexisting hepatic impairment or acute hepatic viral infection may be at higher risk of liver injury. To mitigate potential aminotransferase elevations, administer systemic corticosteroid before and after ITVISMA injection. Prior to ITVISMA injection, assess liver function by clinical examination and laboratory testing. Continue to monitor liver function for at least 3 months after ITVISMA administration, and at other times as clinically indicated. In case hepatic injury is suspected, further testing is recommended. Promptly consult with a gastroenterologist or hepatologist, as necessary.

Please see additional Important Safety Information on page 11, and please click here for Full Prescribing Information, including Boxed WARNING.

STARTING PATIENTS WITH
ONE-TIME-ONLY ITVISMA

ITVISMA® (onasemnogene abeparvovec-brve) is an adeno-associated virus (AAV) vector-based gene replacement therapy for the treatment of spinal muscular atrophy (SMA) in adult and pediatric patients 2 years of age and older. ITVISMA is administered as an intrathecal bolus injection over approximately 1 to 2 minutes.[1]

Patients previously treated with ZOLGENSMA® (onasemnogene abeparvovec-xioi) should not be treated with ITVISMA.[1]

Five key steps to a one-time-only ITVISMA injection[1]:

STEP 1 **Complete initial health assessment and confirm eligibility**

STEP 2 **Store and handle ITVISMA properly**

STEP 3 **Premedicate and plan for administration day**

STEP 4 **Prepare and administer ITVISMA**

STEP 5 **Monitor and postmedicate after ITVISMA administration**

Your Novartis Regional Accounts Associate Director (RAAD) is here to help you and your practice every step of the way! Connect with a RAAD for more information.

Novartis Patient Support™

Novartis Patient Support Case Coordinators provide dedicated guidance and assistance to help patients and caregivers navigate insurance, financial support, and the treatment journey.

To learn more, call 1-855-441-4363, Monday through Friday, 8 AM to 8 PM ET.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS

Thrombocytopenia

Transient decreases in platelet counts were observed within the first week after ITVISMA administration. Monitor platelet counts before ITVISMA injection and on a regular basis afterwards until platelet counts return to baseline.

Please see Indication and Important Safety Information on page 11, and please click here for Full Prescribing Information, including Boxed WARNING.

STEP 1

COMPLETE INITIAL HEALTH ASSESSMENT AND CONFIRM ELIGIBILITY

Testing can be performed at an institution that is already prepared to administer ITVISMA® (onasemnogene abeparvovec-brve) or by a referring physician.

Test for the presence of anti-AAV9 antibodies[1]

- In clinical trials, patients were required to have baseline anti-AAV9 antibody titers of ≤1:50

Additional evaluation and monitoring[1]

- Postpone ITVISMA in patients with active or recent infections, until the infection has resolved, and the patient is clinically stable. Clinical signs and symptoms of infections should not be evident at the time of ITVISMA injection
- Assess vaccination status. Vaccination status should be up-to-date prior to ITVISMA administration
- Assess liver function, including clinical examination and laboratory testing of aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, prothrombin time, partial thromboplastin time (PTT), international normalized ratio (INR), and total bilirubin
- Obtain creatinine and complete blood count, including hemoglobin and platelet count

To begin an ITVISMA prescription, it is recommended that you fax a signed and completed Start Form to Novartis Patient Support™ at 1-855-951-4363, OR upload a completed form at www.ITVISMA-enrollment.com. Questions? Contact 1-855-441-4363.

AAV9, adeno-associated virus serotype 9.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Peripheral Sensory Neuropathy

Peripheral sensory neuropathy has occurred with ITVISMA administration with onset seen at approximately 3 weeks post-injection in clinical studies. Consider complete neurologic evaluation and other testing and/or symptom management based on the patient's clinical presentation.

Please see Indication and Important Safety Information on page 11, and please click here for Full Prescribing Information, including Boxed WARNING.

STEP 2

STORE AND HANDLE ITVISMA PROPERLY

ITVISMA® (onasemnogene abeparvovec-brve) is shipped and delivered frozen. It must be thawed prior to administration.[1]

Delivery and storage[1]

- ITVISMA is shipped and delivered frozen at ≤-60 °C (-76 °F) in a single-dose clear vial
- Upon receipt, immediately place the carton in a refrigerator at 2–8 °C (36–46 °F)
- **DO NOT REFREEZE**
- ITVISMA is stable for 14 days from receipt when stored at 2–8 °C (36–46 °F)

Thawing ITVISMA[1]

Do not use ITVISMA unless thawed. Once thawed, ITVISMA should not be refrozen.

Refrigerator thaw

- **Thaw ITVISMA in the refrigerator for approximately 4 hours**
- If thawed in the refrigerator, remove ITVISMA from refrigerator on day of dosing

—OR—

Room temperature thaw

- Thaw ITVISMA at room temperature for approximately 1 hour

Product administration prep[1]

- When thawed, ITVISMA is a clear to slightly opaque, colorless to faint white liquid, free of particles
- After withdrawal of ITVISMA from the vial, a visual inspection is required
- DO NOT use vials if particulates, cloudiness, or discoloration are visible

Handling[1]

- **DO NOT SHAKE**

STEP 3

PREMEDICATE AND PLAN FOR ADMINISTRATION DAY

Monitoring before treatment[1]

- Ensure required baseline testing for the presence of anti-AAV9 antibodies and liver function assessments (clinical examination and laboratory testing including AST, ALT, albumn, prothrombin time, PTT, INR, and total bilirubin) have been completed, and that creatinine and complete blood count (including hemoglobin and platelet count) have been obtained

Initiate steroids[1]

- **One day prior to ITVISMA® (onasemnogene abeparvovec-brve) injection, begin administration of systemic corticosteroids equivalent to oral prednisolone at 1 mg per kg of body weight per day (mg/kg/day) for a total of 30 days**
- Do not stop systemic corticosteroids abruptly

Evaluate overall health prior to administration[1]

- Due to the increased risk of serious systemic immune response, administer ITVISMA to patients who are clinically stable in their overall baseline health status (eg, hydration and nutritional status, absence of infection, respiratory status) prior to administration
- Clinical signs or symptoms of infection should not be evident at the time of ITVISMA administration

Monitoring and corticosteroids following treatment[1]

- Monitoring should continue following ITVISMA administration. See Step 5 for monitoring instructions
- Treatment with corticosteroids is needed following ITVISMA injection. See Step 5 for postmedication instructions

AAV9, adeno-associated virus serotype 9; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; PTT, partial thromboplastin time.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Thrombotic Microangiopathy

Thrombotic microangiopathy (TMA) may occur with ITVISMA administration and can result in life-threatening or fatal outcomes. Monitor platelet counts on a regular basis following ITVISMA injection, as well as signs and symptoms of TMA. Consult a hematologist and/or nephrologist immediately to manage TMA as clinically indicated.

Please see Indication and Important Safety Information on page 11, and please click here for Full Prescribing Information, including Boxed WARNING.

STEP 4

PREPARE AND ADMINISTER ITVISMA

Prepare ITVISMA® (onasemnogene abeparvovec-brve):

Preparing the syringe[1]

- Each carton of ITVISMA contains a single-dose vial with an extractable volume of not less than 3 mL
- The recommended dose of ITVISMA is 1.2×10^{14} vector genomes (vg)
- ITVISMA should be prepared aseptically
- Prior to intrathecal injection, ITVISMA should be brought to room temperature
- Immediately prior to dosing, draw the content from the vial into the syringe
- Remove air from syringe
- Confirm the dose volume of 3 mL in the syringe
- Cap syringe and deliver to patient injection location

Storing and handling the syringe[1]

- Once dose is drawn into the syringe, it may be held in the refrigerator at 2–8 °C (36–46 °F) for up to 24 hours, including a 5-hour maximum out-of-refrigeration time allowance within the 24-hour period
- Discard the vector-containing syringe if not injected within this time period
- **DO NOT REFREEZE**

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Elevated Cardiac Troponin I

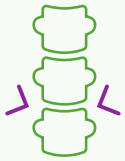
Increases in cardiac troponin I levels have occurred following ITVISMA administration. Consider cardiac evaluation after ITVISMA administration and consult a cardiologist as needed.

Please see Indication and Important Safety Information on page 11, and please click here for Full Prescribing Information, including Boxed WARNING.

STEP 4

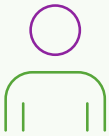
PREPARE AND ADMINISTER ITVISMA (CONT)

Administer ITVISMA® (onasemnogene abeparvovec-brve) as a single-dose intrathecal injection only[1,*]:



Administering the injection[1]

- Prior to administration, remove 3 mL of cerebrospinal fluid (CSF) using a lumbar puncture needle to create space for injection volume
- Administer ITVISMA as an intrathecal bolus injection over approximately 1 to 2 minutes through the lumbar puncture needle
- Place patient in Trendelenburg position (head down at 30 degrees for 15 minutes). Adjust patient positioning and duration based on the patient's clinical status to enhance distribution
- Follow standard post-lumbar puncture care protocols



Administration considerations[1]

- Consider sedation if indicated by the patient's clinical status
- Consider imaging techniques to guide intrathecal injection of ITVISMA
- Evaluate patient prior to and after administration for conditions that may contraindicate lumbar puncture or increase procedural risk to prevent serious complications

*Due to the increased risk of serious systemic immune response, administer ITVISMA to patients who are clinically stable in their overall baseline health status (eg, hydration and nutritional status, absence of infection, respiratory status) prior to administration. Postpone ITVISMA in patients with active or recent infections, until the infection has resolved, and the patient is clinically stable. Clinical signs or symptoms of infection should not be evident at the time of ITVISMA infusion.[1]

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

AAV Vector Integration and Risk of Tumorigenicity

There is a theoretical risk of tumorigenicity due to integration of AAV vector DNA into the genome. The clinical relevance of individual integration events is unknown, but it is acknowledged that individual integration events could potentially contribute to a risk of tumorigenicity. Report cases of tumor development in patients who received ITVISMA to Novartis Gene Therapies, Inc. at 1-833-828-3947.

Please see Indication and Important Safety Information on page 11, and please click here for Full Prescribing Information, including Boxed WARNING.

STEP 5

MONITOR AND POSTMEDICATE AFTER ITVISMA ADMINISTRATION

Continue to monitor liver function for at least 3 months and platelet count for at least 1 month after ITVISMA® (onasemnogene abeparvovec-brve) administration, and at other times as clinically indicated.[1]

Liver function[1]

- Hepatotoxicity, with elevated ALT and/or AST levels, has occurred with ITVISMA
- In order to mitigate potential aminotransferase elevations, administer systemic corticosteroid before and after ITVISMA injection. The recommended corticosteroid regimen is detailed in the table on page 10 and in the Prescribing Information
- Monitor AST, ALT, and total bilirubin weekly for the month (or longer based on liver function) after ITVISMA administration and during the corticosteroid taper period
- If the patient is clinically stable with unremarkable findings at the end of the corticosteroid taper period, continue to monitor liver function every other week for another month. Tapering of systemic corticosteroids should not be considered until AST/ALT levels are less than 2 × upper limit of normal (ULN)

Platelet count[1]

- Transient decreases in platelet counts were observed within the first week after ITVISMA administration. The platelet counts are expected to return to baseline 2 weeks following ITVISMA injection
- Monitor platelet counts before ITVISMA injection and on a regular basis afterwards (at least weekly for the first month and as clinically indicated until platelet counts return to baseline)
- Also monitor for signs and symptoms of thrombotic microangiopathy (TMA), such as hypertension, bruising easily, seizures, or decreased urine output. In case these signs and symptoms occur in the presence of thrombocytopenia, further diagnostic evaluation for hemolytic anemia and renal dysfunction should be promptly undertaken
- If clinical signs, symptoms, and/or laboratory findings consistent with TMA occur, consult a hematologist and/or nephrologist immediately to manage TMA as clinically indicated

ALT, alanine aminotransferase; AST, aspartate aminotransferase.

STEP 5

MONITOR AND POSTMEDICATE AFTER ITVISMA ADMINISTRATION (CONT)

Schedule of assessments before and after administration:

Baseline assessments prior to administration[1]

Assess vaccination status (vaccination status should be up-to-date prior to ITVISMA administration) and liver function (clinical examination and laboratory testing, including AST, ALT, albumin, prothrombin time, PTT, INR, and total bilirubin); obtain creatinine and complete blood count (including hemoglobin and platelet count); and perform baseline testing for the presence of anti-AAV9 antibodies.

Monitoring after ITVISMA administration[1]

Test	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	Wk 7	Wk 8	Wk 9	Wk 10	Wk 11	Wk 12
Liver function*	**2 months or longer, until the patient is clinically stable with unremarkable findings.**								Continue to monitor liver function every other week for another month.‡			
	Monitor AST, ALT, and total bilirubin weekly for the month (or longer) after ITVISMA administration and during the corticosteroid taper period.											
	✓	✓	✓	✓	✓	✓	✓	✓		✓		✓
	Monitor patients with worsening liver function test results and/or signs or symptoms of acute illness (eg, vomiting, deterioration in health). In case hepatic injury is suspected, further testing is recommended (eg, albumin, prothrombin time, PTT and INR). Promptly consult with a gastroenterologist or hepatologist, as necessary.											
Platelet count§	Monitor at least weekly for the first month.				Continue monitoring as clinically indicated until platelet counts return to baseline.							
	✓	✓	✓	✓								
Consider cardiac evaluation after ITVISMA administration and consult a cardiologist as needed.[1]												

*Monitor liver function for at least 3 months or longer.[1]
†The corticosteroid taper period occurs over the next 28 days or longer if needed.[1]
‡If the patient is clinically stable with unremarkable findings at the end of the corticosteroid taper period. Tapering of systemic corticosteroids should not be considered until AST/ALT levels are less than 2 × ULN.[1]
§Monitor platelet counts as well as signs and symptoms of TMA, such as hypertension, bruising easily, seizures, or decreased urine output.[1]

Due to the increased risk of serious systemic immune response, administer ITVISMA® (onasemnogene abeparvovec-brve) to patients who are clinically stable in their overall baseline health status (eg, hydration and nutritional status, absence of infection, respiratory status) prior to administration. Postpone ITVISMA in patients with active or recent infections, until the infection has resolved, and the patient is clinically stable. Clinical signs or symptoms of infection should not be evident at the time of ITVISMA administration.[1]

AAV9, adeno-associated virus serotype 9; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; PTT, partial thromboplastin time; ULN, upper limit of normal; Wk, week; ✓, monitoring performed.

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE EVENTS

The most common adverse reactions that occurred in ≥2% of patients treated with ITVISMA were upper respiratory tract infection, pyrexia, upper gastrointestinal symptoms, hepatic enzymes increased, headache, dizziness, pain in extremity, thrombocytopenia, and sensory disturbance.

Please see Indication and Important Safety Information on page 11, and please click here for Full Prescribing Information, including Boxed WARNING.

STEP 5

MONITOR AND POSTMEDICATE AFTER ITVISMA ADMINISTRATION (CONT)

Treat with systemic corticosteroids prior to and following ITVISMA injection.[1]

Recommended corticosteroid regimen prior to and following ITVISMA® (onasemnogene abeparvovec-brve) injection[1]	
Pre-injection	
24 hours prior to ITVISMA injection	**Oral prednisolone 1 mg/kg/day (or equivalent)**
Post-injection	
30 days (including the day of ITVISMA administration)	**Oral prednisolone 1 mg/kg/day (or equivalent)**
Followed by 28 days: ***For patients with unremarkable findings (normal clinical exam, total bilirubin, and ALT and AST levels below 2 × ULN)*** **or** ***For patients with liver function abnormalities at the end of the 30-day period: continue until the AST and ALT values are both below 2 × ULN and all other assessments return to normal range, and then taper the corticosteroid dose over the next 28 days or longer if needed.***	**Systemic corticosteroids should be tapered gradually** **Taper prednisolone (or equivalent)** **Systemic corticosteroids (or equivalent to oral prednisolone 1 mg/kg/day)** **Systemic corticosteroids should be tapered gradually**

If at any time patients do not respond adequately to the equivalent of 1 mg/kg/day oral prednisolone, based on the patient's clinical course, obtain prompt consultation with a gastroenterologist or hepatologist and consider adjustment to the recommended corticosteroid regimen, including increased dose, longer duration or prolongation of corticosteroid taper.[1]

If oral corticosteroid therapy is not tolerated or not effective, consider intravenous corticosteroids, as clinically indicated.[1]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal.

Reference: 1. ITVISMA. Prescribing information. Novartis Gene Therapies, Inc.

Please see Indication and Important Safety Information on page 11, and please click here for Full Prescribing Information, including Boxed WARNING.

Indication and Important Safety Information for ITVISMA® (onasemnogene abeparvovec-brve) suspension for intrathecal injection

INDICATION

ITVISMA is indicated for the treatment of spinal muscular atrophy (SMA) in adult and pediatric patients 2 years of age and older with confirmed mutation in *survival motor neuron 1* (*SMN1*) gene.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: Serious Liver Injury

Acute serious liver injury can occur with ITVISMA. Hepatotoxicity, with elevated alanine transaminase (ALT) and/or aspartate transaminase (AST) levels, has occurred with ITVISMA. Patients with preexisting hepatic impairment or acute hepatic viral infection may be at higher risk of liver injury. To mitigate potential aminotransferase elevations, administer systemic corticosteroid before and after ITVISMA injection. Prior to ITVISMA injection, assess liver function by clinical examination and laboratory testing. Continue to monitor liver function for at least 3 months after ITVISMA administration, and at other times as clinically indicated. In case hepatic injury is suspected, further testing is recommended. Promptly consult with a gastroenterologist or hepatologist, as necessary.

WARNINGS AND PRECAUTIONS

Thrombocytopenia
Transient decreases in platelet counts were observed within the first week after ITVISMA administration. Monitor platelet counts before ITVISMA injection and on a regular basis afterwards until platelet counts return to baseline.

Peripheral Sensory Neuropathy
Peripheral sensory neuropathy has occurred with ITVISMA administration with onset seen at approximately 3 weeks post-injection in clinical studies. Consider complete neurologic evaluation and other testing and/or symptom management based on the patient's clinical presentation.

Thrombotic Microangiopathy
Thrombotic microangiopathy (TMA) may occur with ITVISMA administration and can result in life-threatening or fatal outcomes. Monitor platelet counts on a regular basis following ITVISMA injection, as well as signs and symptoms of TMA. Consult a hematologist and/or nephrologist immediately to manage TMA as clinically indicated.

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Please click here for Full Prescribing Information.

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