AMONDYS 45

(casimersen) 100 mg/2 mL injection

DOSING & ADMINISTRATION GUIDE

AMONDYS45.com

INDICATION

AMONDYS 45 is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 45 skipping. This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with AMONDYS 45. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

Nicholas, AGE 12
DELETION OF EXON 44

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

Known hypersensitivity to casimersen or any of the inactive ingredients. Instances of hypersensitivity including angioedema and anaphylaxis have occurred.

WARNINGS AND PRECAUTIONS

Hypersensitivity: Hypersensitivity reactions, including angioedema and anaphylaxis, have occurred in patients who were treated with AMONDYS 45. If a hypersensitivity reaction occurs, institute appropriate medical treatment, and consider slowing the infusion, interrupting, or discontinuing the AMONDYS 45 infusion and monitor until the condition resolves.

Kidney Toxicity: Kidney toxicity was observed in animals who received casimersen. Although kidney toxicity was not observed in the clinical studies with AMONDYS 45, kidney toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Kidney function should be monitored in patients taking AMONDYS 45. Because of the effect of reduced skeletal muscle mass on creatinine measurements, creatinine may not be a reliable measure of kidney function in DMD patients. Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting AMONDYS 45. Consider also measuring glomerular filtration rate using an exogenous filtration marker before starting AMONDYS 45. During treatment, monitor urine dipstick every month, and serum cystatin C and urine protein-to-creatinine ratio (UPCR) every three months. Only urine expected to be free of excreted AMONDYS 45 should be used for monitoring of urine protein. Urine obtained on the day of AMONDYS 45 infusion prior to the infusion, or urine obtained at least 48 hours after the most recent infusion, may be used. Alternatively, use a laboratory test that does not use the reagent pyrogallol red, as this reagent has the potential to cross react with any AMONDYS 45 that is excreted in the urine and thus lead to a false positive result for urine protein.

If a persistent increase in serum cystatin C or proteinuria is detected, refer to a pediatric nephrologist for further evaluation.

Adverse Reactions: Adverse reactions occurring in at least 20% of patients treated with AMONDYS 45 and at least 5% more frequently than in the placebo group were (AMONDYS 45, placebo): upper respiratory infections (65%, 55%), cough (33%, 26%), pyrexia (33%, 23%), headache (32%, 19%), arthralgia (21%, 10%), and oropharyngeal pain (21%, 7%).

Other adverse reactions that occurred in at least 10% of patients treated with AMONDYS 45 and at least 5% more frequently than in the placebo group were: ear pain, nausea, ear infection, post-traumatic pain, and dizziness and light-headedness.

Please see the full Prescribing Information for AMONDYS 45 (casimersen).

AMONDYS 45 has met the full statutory standards for safety and effectiveness, and as such, is not considered investigational or experimental.[1]

AMONDYS 45
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Colin, AGE 11
DELETIONS OF EXONS 12-44

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AMONDYS 45 (casimersen) 100 mg/2 mL injection

IMPORTANT INFORMATION[2]

Patient eligibility. AMONDYS 45 should only be administered to patients who have a confirmed mutation of the *DMD* gene that is amenable to skipping exon 45.

Monitoring to assess safety. Measurement of glomerular filtration rate prior to initiation of AMONDYS 45 and monitoring for kidney toxicity during treatment is recommended.

The recommended dose of AMONDYS 45 is 30 mg/kg administered once weekly as a 35- to 60-minute intravenous (IV) infusion via an in-line 0.2 micron filter. If a dose of AMONDYS 45 is missed, it may be administered as soon as possible after the scheduled dose.

Infusion-site care. Application of a topical anesthetic cream to the infusion site prior to administration of AMONDYS 45 may be considered.

Hypersensitivity reactions. Advise patients and/or caregivers that hypersensitivity reactions, including angioedema and anaphylaxis, have occurred in patients who were treated with AMONDYS 45. Instruct them to seek immediate medical care should they experience signs and symptoms of hypersensitivity.

Kidney toxicity. Inform patients that nephrotoxicity has occurred with drugs similar to AMONDYS 45. Advise patients of the importance of monitoring for kidney toxicity by their healthcare providers during treatment with AMONDYS 45.

How supplied. AMONDYS 45 injection is supplied in single-dose vials containing 100 mg/2 mL (50 mg/mL) casimersen. The solution is a clear to slightly opalescent, colorless liquid, and may contain trace amounts of small, white to off-white amorphous particles.

Storage. Store AMONDYS 45 at 2 °C to 8 °C (36 °F to 46 °F). Do not freeze. Store AMONDYS 45 in the original carton until ready for use to protect from light.

IMPORTANT SAFETY INFORMATION

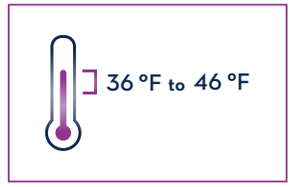
Adverse Reactions: Adverse reactions occurring in at least 20% of patients treated with AMONDYS 45 and at least 5% more frequently than in the placebo group were (AMONDYS 45, placebo): upper respiratory infections (65%, 55%), cough (33%, 26%), pyrexia (33%, 23%), headache (32%, 19%), arthralgia (21%, 10%), and oropharyngeal pain (21%, 7%).

BEFORE THE INFUSION

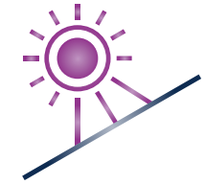
PROPER STORAGE AND HANDLING OF AMONDYS 45[2]

Once you receive AMONDYS 45 at your facility, be sure to store it according to proper procedures:

Store AMONDYS 45 at 2 °C to 8 °C (36 °F to 46 °F)



Protect from light and store in the original carton until ready for use



Do not freeze

Other adverse reactions that occurred in at least 10% of patients treated with AMONDYS 45 and at least 5% more frequently than in the placebo group were: ear pain, nausea, ear infection, post-traumatic pain, and dizziness and light-headedness.

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AMONDYS 45 (casimersen) 100 mg/2 mL injection

AMONDYS 45 DOSING CALCULATIONS[2]

To calculate the dose of AMONDYS 45 you will need to:

STEP 1 Calculate the patient dose in mg:
Patient weight (kg) x 30 mg/kg = total dose in mg of AMONDYS 45

STEP 2 Calculate the volume in mL:

Total mg of AMONDYS 45 needed	**÷**	**50 mg/mL**	**=**	**Total volume in mL** of AMONDYS 45 needed

STEP 3 Calculate the number of single-dose vials the patient needs:
Total mL needed ÷ 2 = # of 2 mL vials

DOSING CALCULATION EXAMPLE BASED ON 33.5 KG PATIENT

STEP 1 Calculate the dose in mg:
33.5 kg x 30 mg/kg = 1,005 mg

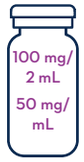
STEP 2 Calculate the volume in mL:
1,005 mg ÷ 50 mg/mL = 20.1 mL

STEP 3 Calculate the number of single-dose vials:
20.1 mL = 11 (eleven) 2-mL vials

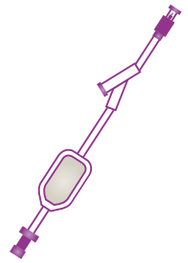
NECESSARY SUPPLIES[2]

To infuse AMONDYS 45 you will need:

AMONDYS 45
2-mL single-dose vials containing
100 mg casimersen



0.9% sodium chloride injection, USP,
(normal saline solution) infusion bag
(volume of 100-150 mL)



0.2 micron filter

A syringe fitted with a 21-gauge
or smaller bore non-coring needle

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PREPARING AMONDYS 45 USING ASEPTIC TECHNIQUE

PREPARE AMONDYS 45 ACCORDING TO THESE STEPS

STEP 1[2]

Complete the dosing calculation.
See page 8 of this brochure for information on how to complete the dosing calculation.

STEP 2[2]

AMONDYS 45 is administered once weekly as a 35- to 60-minute intravenous (IV) infusion via an in-line 0.2 micron filter.

Application of a topical anesthetic cream to the infusion site prior to administration of AMONDYS 45 may be considered.

STEP 3[3]

Assess the patient's IV or port for patency prior to removing any vials from the refrigerator. If IV access is adequate, remove the appropriate number of vials from the refrigerator and allow them to warm to room temperature. Do not microwave vials.

STEP 4[2]

Once at room temperature, mix the contents of each vial by gently inverting 2 or 3 times. Do not shake. Visually inspect each vial of AMONDYS 45. AMONDYS 45 is a clear to slightly opalescent, colorless liquid, and may contain trace amounts of small, white to off-white amorphous particles. Do not use if the solution is cloudy, discolored, or contains extraneous particulate matter other than trace amounts of small, white to off-white amorphous particles. If there is an issue with the solution, please report the issue to Sarepta at 1-888-SAREPTA (1-888-727-3782).

STEP 5[2]

With a syringe fitted with a 21-gauge or smaller bore non-coring needle, withdraw the calculated volume of AMONDYS 45 from the appropriate number of vials.

STEP 6[2]

Dilute the withdrawn AMONDYS 45 in 0.9% sodium chloride injection, USP, to make a total volume of 100 to 150 mL. Before diluting AMONDYS 45, withdraw excess saline from the bag, if needed. Gently invert 2 to 3 times to mix. Do not shake. Visually inspect the diluted solution. Do not use if the solution is cloudy, discolored, or contains extraneous particulate matter other than trace amounts of small, white to off-white amorphous particles.

AMONDYS 45 contains no preservatives and should be administered immediately after dilution. Complete infusion of diluted AMONDYS 45 within 4 hours of dilution. If immediate use is not possible, the diluted product may be stored for up to 24 hours at 2 °C to 8 °C (36 °F to 46 °F). Do not freeze. Discard unused AMONDYS 45.

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INFUSING AMONDYS 45

ADMINISTER AMONDYS 45 ACCORDING TO THESE STEPS

STEP 7[2,4]

- Flush the patient's intravenous access line with 0.9% sodium chloride injection, USP, prior to infusion.
- Infuse the diluted AMONDYS 45 over 35 to 60 minutes via an in-line 0.2 micron filter. Do not mix other medications with AMONDYS 45 or infuse other medications concomitantly via the same intravenous access with AMONDYS 45.
- If a hypersensitivity reaction occurs, consider slowing the infusion, interrupting, or discontinuing the AMONDYS 45 therapy.
- After completion of the infusion, flush the intravenous access line with 0.9% sodium chloride injection, USP, to allow the entire dose, including the contents of the intravenous access line, to be administered.
- In cases where AMONDYS 45 is administered into a venous access port, after administration of the drug and flushing with normal saline, the port may be flushed with heparin prior to de-access.

ADDITIONAL IMPORTANT INFORMATION

When administering AMONDYS 45 to patients with implanted infusion devices, access the device following the manufacturer's instructions for use to minimize the potential for infection.

AFTER THE INFUSION

STEP 8[2]

Once you have completed the infusion, discard any unused product.

To report suspected adverse reactions, contact Sarepta Therapeutics, Inc. at 1-888-SAREPTA (1-888-727-3782) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

IMPORTANT SAFETY INFORMATION

Hypersensitivity:

- Hypersensitivity reactions, including angioedema and anaphylaxis, have occurred in patients who were treated with AMONDYS 45.
- If a hypersensitivity reaction occurs, institute appropriate medical treatment, and consider slowing the infusion, interrupting, or discontinuing the AMONDYS 45 infusion and monitor until the condition resolves.

Kidney Toxicity:

- Kidney toxicity was observed in animals who received casimersen. Although kidney toxicity was not observed in the clinical studies with AMONDYS 45, kidney toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides.
- Kidney function should be monitored in patients taking AMONDYS 45. Because of the effect of reduced skeletal muscle mass on creatinine measurements, creatinine may not be a reliable measure of kidney function in DMD patients.
- Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting AMONDYS 45. Consider also measuring glomerular filtration rate using an exogenous filtration marker before starting AMONDYS 45.
- During treatment, monitor urine dipstick every month, and serum cystatin C and urine protein-to-creatinine ratio (UPCR) every three months. Only urine expected to be free of excreted AMONDYS 45 should be used for monitoring of urine protein. Urine obtained on the day of AMONDYS 45 infusion prior to the infusion, or urine obtained at least 48 hours after the most recent infusion, may be used. Alternatively, use a laboratory test that does not use the reagent pyrogallol red, as this reagent has the potential to cross react with any AMONDYS 45 that is excreted in the urine and thus lead to a false positive result for urine protein.
- If a persistent increase in serum cystatin C or proteinuria is detected, refer to a pediatric nephrologist for further evaluation.

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SAREPTASSIST

Support, By Your Patients' Side

SareptAssist is a personalized support program here to help your patients on their treatment journey. Our dedicated Case Managers can help patients, families, and caregivers:

- Understand treatment requirements
- Consider financial assistance options
- Explore insurance benefits
- Prepare for treatment
- Find helpful resources
- Get ongoing education and support

SareptAssist Is Here for Your Patients. Get Connected!
Call 1-888-SAREPTA (1-888-727-3782)
We're available Monday through Friday, 8:30 am – 6:30 pm ET.

Spanish-speaking Case Managers and interpreters of other languages are available.

References: 1. Federal Register Vol 57, No. 239 December 11, 1992. **2.** AMONDYS 45 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc. 2023. **3.** Infusion Nurses Society. Infusion Therapy Standards of Practice 2016, Online edition. *Journal of Infusion Nursing*. Accessed on November 6, 2020. https://library.ins1.org/hai13r/ **4.** Data on file. Sarepta Therapeutics, Inc.

SAREPTA THERAPEUTICS

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04/23 C-SRP-45-US-0031

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