Drug Monograph

Drug Name: **Amondys 45™ (casimersen) Vial**
Drug Class: **Antisense Oligonucleotide Agents**
Prepared For: MO HealthNet
Prepared By: Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms:	Amondys 45 is available as a single-dose vial containing 100 mg of casimersen for intravenous injection.
Manufacturer:	Manufactured for: Sarepta Therapeutics, Inc., Cambridge, MA 02142.
Summary of Findings:	The efficacy and safety of Amondys 45 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. Amondys 45 was given approval under the accelerated approval based on an increase in dystrophin production in skeletal muscle observed in one clinical trial enrolling 43 patients. There was a mean change in dystrophin levels from baseline of 0.81 ($p<0.001$). This trial is ongoing.

Status Recommendation:	☒ Clinical Edit ☐ Open Access	☐ PA Required ☐ PDL
Type of PA Criteria:	☒ Appropriate Indications ☐ No PA Required	☐ Non-Preferred ☐ Preferred

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [1,2]

Duchenne muscular dystrophy (DMD) is a rare genetic disorder caused by a genetic mutation in the *DMD* gene that prevents the body from producing dystrophin, a protein that muscles need to work properly. DMD occurs primarily in males and is inherited in an X-linked recessive pattern. The prevalence of DMD in Europe and North America is 6 per 100,000 individuals. Symptoms of DMD include progressive weakness and loss of both skeletal and heart muscle.

Dosage Form [3]

Amondys 45 is available as a single-dose vial containing 100 mg of casimersen for intravenous injection.

Manufacturer [3]

Manufactured for: Sarepta Therapeutics, Inc., Cambridge, MA 02142.

Indication(s) [3]

Amondys 45 is indicated for the treatment of 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.

Clinical Efficacy [3,4,5] (mechanism of action/pharmacology, comparative efficacy)

Amondys 45 is an antisense oligonucleotide that binds to exon 45 of dystrophin pre-messenger RNA (pre-mRNA), resulting in exclusion of this exon during mRNA processing. Exon 45 skipping allows for production of an internally truncated dystrophin protein in patients with genetic mutation that are amendable to exon 45 skipping.

Pharmacokinetics:

Protein Binding	8.4% to 31.6%
Volume of Distribution	367 mL/kg
Metabolism	Not metabolized
Excretion	Renal: >90%
Half-life	3.5 hours

Clinical Trials Experience:

STUDY 1 DESIGN (ESSENCE)	Randomized 2:1, double-blind, placebo-controlled, multicenter (n=43) (on-going)
INCLUSION CRITERIA	• Genotypically confirmed DMD, with genetic deletion amenable to exon 45 or exon 53 • Stable dose of oral corticosteroids for at least 24 weeks • Intact right and left biceps or 2 alternative upper muscle groups • Mean 6MWT ≥ 300 meters or ≤ 450 meters • Stable pulmonary function: forced vital capacity equal to or greater than 50% predicted
EXCLUSION CRITERIA	• Treatment with gene therapy at any time • Current or previous treatment with any other experimental treatment • Major surgery within 3 months • Presence of other clinically significant illness
TREATMENT REGIMEN	Patients were randomized 2:1 to receive Amondys 45 (n=27) 30 mg/kg/week via IV infusion for up to 96 weeks or placebo (n=16). Interim results at 48 weeks were reviewed for the FDA accelerated approval.
RESULTS	The interim measure of efficacy was assessed based on a change from baseline in the dystrophin protein level measured as a percentage of the dystrophin level in healthy subjects at week 48. The change in dystrophin levels from baseline was 0.81 for the Amondys 45-treated patients vs 0.22 for the placebo patients (p<0.001).
SAFETY	Discussed in the Adverse Effects section below.

Abbreviations: 6MWT= 6-minute walk test

Contraindications [3,4]

- None

Warnings and Precautions [3,4]

- Kidney Toxicity: Based on animal data, may cause kidney toxicity. Kidney function should be monitored. Creatinine may not be a reliable measure of renal function in DMD patients.

Adverse Effects [3,4]

Most common, ≥ 20%	(n =57) %
Upper Respiratory Tract Infections	65
Cough	33
Pyrexia	33
Headache	33
Arthralgia	21
Oropharyngeal Pain	21

Drug Interactions [3,4]

- Casimersen has a low potential for clinically relevant drug-drug interactions with major CYP enzymes and transporters.

Dosage and Administration [3,4]

30 mg/kg once weekly as a 35 to 60-minute intravenous infusion via an in-line 0.2 micron filter.

Cost

Generic Name	Brand Name	Manufacturer	Dose	Cost**/Dose
Casimersen	Amondys 45	Sarepta Therapeutics, Inc.	30 mg/kg once weekly	$33,600 for a 70 kg patient

** Wholesale Acquisition Cost

Conclusion

Amondys 45, an antisense oligonucleotide, 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. Amondys 45 was given FDA accelerated approval based on an increase in dystrophin production in skeletal muscle observed in one clinical trial. The most common adverse reactions occurring with an incidence of >20% were upper respiratory tract infection, cough, pyrexia, headache, arthralgia and oropharyngeal pain.

Recommendation

The MO Healthnet Division recommends adding this drug to the current Duchenne muscular dystrophy clinical edit.

References

1) Muscular Dystrophy Association. Duchenne Muscular Dystrophy. www.mda.org. Accessed May 2021.
2) IPD Analytics. New drug review- Amondys 45. ipdanalytics.com. Accessed May 2021.
3) Amondys 45 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; 2021.
4) Amondys 45: Drug Information. Lexi-Drugs. Wolters Kluwer Clinical Drug Information Inc. Accessed May 2021.
5) A Double-Blind, Placebo-Controlled, Multi-Center Study With an Open-Label Extension to Evaluate the Efficacy and Safety of SRP-4045 and SRP-4053 in Patients With Duchenne Muscular Dystrophy. NCT02500381. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02500381?cond=02500381&draw=2&rank=1. Accessed May 2021.

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Date: May 9, 2021