VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Muscular Dystrophy – Amondys 45 Utilization Management Medical Policy
- Amondys 45™ (casimersen intravenous infusion – Sarepta)

REVIEW DATE: 02/19/2025

OVERVIEW

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.[1] This indication was granted accelerated approval based on an increase in dystrophin in skeletal muscle observed in patients treated with Amondys 45. The prescribing information notes that continued FDA-approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

Guidelines

Amondys 45 is not addressed in the guidelines for the diagnosis and management of DMD available from the DMD Care Considerations Working Group (2018).[2] Glucocorticoids slow decline in muscle strength and function in DMD and should be considered for all patients with DMD. Exondys 51 (eteplirsen intravenous infusion) is mentioned as an emerging product, approved by an accelerated pathway for those with a mutation in the dystrophin gene amenable to exon 51 skipping.

POLICY STATEMENT

The prescribing information for Amondys 45 states that approval is based on dystrophin production in a limited number of patients (n = 27 treated with Amondys 45) with DMD, but continued approval may be contingent upon a confirmatory trial. Due to inadequate clinical efficacy data, **approval is not recommended** for Amondys 45.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

None.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Amondys 45 is not recommended in the following situations:

1. **Duchenne Muscular Dystrophy.** Approval is not recommended due to the unclear clinical benefit of Amondys 45 and lack of clinical efficacy data. Shortcomings of the clinical data with Amondys 45 are numerous. In the pivotal trial, a minimal increase in dystrophin level was noted, but has not been correlated with a clinical benefit. Available data from the pivotal study did not provide any information to determine if Amondys 45 provides a benefit in regard to cardiac and respiratory complications which contribute greatly to morbidity and mortality in patients with DMD. Further, there are concerns of renal toxicity with utilization of Amondys 45, and available data do not support optimal timing for initiation or discontinuation of Amondys 45. Amondys 45 has not been proven to alter or delay disease progression in patients with DMD amenable to exon 45 skipping. A systematic review and meta-analysis of other exon skipping therapies (i.e., Exondys 51, drisapersen) did not show benefit of these

therapies for DMD.[3] The FDA has required a post-marketing trial to verify the clinical efficacy of Amondys 45; patients are still being recruited for the pivotal Phase III ESSENCE study, to further evaluate safety and efficacy in ambulatory boys with DMD.[4]

Amondys 45 is under evaluation in one ongoing, Phase III pivotal study (ESSENCE) in patients with DMD amenable to exon 45 skipping.[1] The primary endpoint is the effect of Amondys 45 on the change from baseline in the total distance walked during the 6-Minute Walk Test (6MWT) at Week 96.[4] Functional outcomes are among the secondary endpoints. In an interim analysis from 43 evaluable patients (n = 27 treated with Amondys 45; n = 16 treated with placebo), the proportion of normal dystrophin protein level was higher at Week 48 with Amondys 45 (1.74% of normal at Week 48 vs. 0.93% of normal at baseline) vs. placebo (0.76% of normal at Week 48 vs. 0.54% of normal at baseline) [P = 0.004 for Amondys 45 vs. placebo].[1] Results from the primary endpoint (6MWT) and functional outcomes have not been reported. The estimated study completion date is October 2025.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Amondys 45 intravenous infusion [prescribing information]. Cambridge, MA: Sarepta; July 2024.
2. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol*. 2018;17(3):251-267.
3. Shimizu-Motohashi Y, Murakami T, Kimura E, et al. Exon skipping for Duchenne muscular dystrophy: a systematic review and meta-analysis. *Orphanet J Rare Dis*. 2018;13(1):93.
4. US National Institutes of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2025 Feb 15]. Available from: https://clinicaltrials.gov/ct2/show/NCT02500381. Search term: NCT02500381.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/15/2023
Annual Revision	No criteria changes	02/14/2024
Annual Revision	No criteria changes	02/19/2025