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MEDICAL POLICY

Amondys 45 (casimersen)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

This Medical Policy document describes the status of medical technology at the time the document was developed. Since that time, new technology may have emerged or new medical literature may have been published. This Medical Policy will be reviewed regularly and be updated as scientific and medical literature becomes available.

DESCRIPTION

Amondys 45 (casimersen), an antisense oligonucleotide, is indicated for treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping. It is administered once weekly as an intravenous (IV) infusion.

This indication was approved by the Food and Drug Administration (FDA) in February 2021 under accelerated approval based on the surrogate endpoint of an increase in dystrophin in skeletal muscle observed in patients treated with Amondys 45 (casimersen). A clinical benefit of Amondys 45 (casimersen) has not been established.

POLICY

Amondys 45 (casimersen) is considered **not medically necessary** for all indications, including the treatment for DMD, due to insufficient evidence to demonstrate clinical efficacy.

CLINICAL RATIONALE

Amondys 45 (casimersen) is an exon-skipping therapy that targets dystrophin pre-messenger ribonucleic acid (mRNA) and induces skipping of mutated exons of the DMD gene that disrupt downstream protein synthesis and lead to nonfunctional or absent dystrophin. Skipping mutated exons results in restoration of small amount of dystrophin. It is unknown whether an increase in dystrophin will lead to clinical improvement in patients with DMD. Amondys 45 (casimersen) is indicated for the treatment of DMD in patients with a confirmed mutation amenable to exon 45 skipping which accounts for approximately 8% of patients with DMD. It is the fourth antisense oligonucleotide approved by the FDA for the treatment of DMD and the only agent indicated for patients with a confirmed DMD mutation that is amenable to exon 45 skipping.

Clinical Studies

FDA approval of Amondys 45 (golodirsen) was based on unpublished interim results of 43 evaluable patients at 48 weeks in the ESSENCE trial. ESSENCE is an ongoing phase III, multinational, randomized, double-blind, placebo-controlled, multi-arm trial designed to evaluate the efficacy and safety of both Amondys 45 (casimersen) (N = 111) and Vyondys 53 (golodirsen) (N = 111) in male patients 7 years to 13 years of age with DMD mutations amenable to skipping exon 45 or exon 53, respectively. Patients with mutations in the DMD gene amenable to exon 45 skipping who were receiving a stable dose of oral corticosteroids for at least 24 weeks prior to trial initiation were randomized to receive once-weekly intravenous infusion of Amondys 45 (casimersen) dosed at 30 mg/kg or placebo for 96 weeks, followed by an open-label extension period, in which all patients will receive open-label active treatment for 48 weeks. The interim analysis was performed at 48 weeks on data from biopsies of bicep muscle at baseline and on-treatment for 43 evaluable patients; these patients had a mean age of 9 years and were 86% white. In patients treated with Amondys 45 (casimersen), the mean dystrophin protein as % of normal dystrophin measured by Western blot increased to 1.74% of normal at 48 weeks compared with their baseline mean of 0.93% of normal (i.e., 0.81% increase from baseline; $p < 0.001$; n = 27). In the placebo arm, the mean dystrophin protein was 0.54% of normal at baseline and 0.76% of normal at 48 weeks (i.e., 0.22% increase from baseline; p = not significant; n = 16). The between-group difference in the change of dystrophin level at 48 weeks was 0.59% ($p = 0.004$), indicating that Amondys 45 (casimersen) significantly increased dystrophin levels compared with placebo at 48 weeks in male patients with DMD mutations amenable to exon 45 skipping. Additionally, of the 22 patients treated with Amondys 45 (casimersen) who have been tested for increased exon-skipping mRNA using reverse transcription polymerase chain reaction (RT-PCR), all have displayed an increase in skipping exon 45 ($p < 0.001$) over their baseline levels. A positive correlation between exon 45 skipping and dystrophin production was observed (Spearman rank correlation = 0.635; $p < 0.001$). Although the ESSENCE trial included clinical benefit assessments such as 6MWT, data are not available currently.

Although kidney toxicity was not observed in the Amondys 45 clinical studies, 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. The most common side effects observed in DMD patients treated with Amondys 45 were upper respiratory tract infections, cough, fever, headache, joint pain, and throat pain. Other adverse reactions that occurred in at least 10% of patients treated with Amondys 45, and that were reported at a rate at least 5% more frequently in the Amondys 45 group than in the placebo group, were ear pain, nausea, ear infection, posttraumatic pain, and dizziness and light-headedness.

Amondys 45 was approved based on a surrogate marker of observed increase in dystrophin in skeletal muscle, but it is unknown whether that increase is clinically significant or if it results in an improvement in functional outcome. The trial was not designed to evaluate long-term safety, and no functional outcome, including improved motor function, has been found.

As part of the FDA's accelerated approval of Amondys 45, a post-marketing confirmatory study (ESSENCE) is currently ongoing. It is a phase 3, double-blind placebo-controlled, multicenter study that must assess whether Amondys 45 improves motor function of DMD patients with a confirmed mutation of the dystrophin gene amenable to exon 45 skipping. It is expected to conclude by 2024. If a clinical benefit is not found, the FDA may withdraw approval.

In summary, the clinical benefit of treatment for DMD with Amondys 45 (casimersen) has not been demonstrated. The establishment of a clinical benefit, including improved motor function and pulmonary function, is warranted in on-going clinical trials. The following conclusion is also stated in the FDA prescribing information, "Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials."

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- C9075 Injection, casimersen, 10 mg (termed 10-1-2021)
- J1426 Injection, casimersen, 10 mg (effective 10-1-2021)

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*Some content reprinted from CVS Health

POLICY HISTORY

Policy #: 05.04.35
Policy Creation: April 2021
Reviewed: February 2022
Revised:
Current Effective Date: May 20, 2021