Vyondys 53 (golodirsen)

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

Vyondys 53 (golodirsen), 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 53 skipping. It is administered once weekly as an intravenous (IV) infusion and may be used as monotherapy or in combination with corticosteroids.

This indication was approved by the Food and Drug Administration (FDA) in December 2019 under accelerated approval based on the surrogate endpoint of an increase in dystrophin in skeletal muscle observed in patients treated with Vyondys 53 (golodirsen). A clinical benefit of Vyondys 53 (golodirsen) has not been established.

POLICY

Vyondys 53 (golodirsen) is considered **not medically necessary** for all indications, including the treatment for DMD, due to insufficient evidence to demonstrate clinical efficacy.

CLINICAL RATIONALE

Vyondys 53 (golodirsen) 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. Vyondys 53 (golodirsen) is indicated for the treatment of DMD in patients with a confirmed mutation amenable to exon 53 skipping which accounts for 8% of DMD population.

Clinical Studies

FDA approval of Vyondys 53 (golodirsen) was based on an increase in a surrogate marker, dystrophin production in skeletal muscle during a single two-part clinical study in patients who had a confirmed mutation of the DMD gene that was amenable to exon 53 skipping. The trial was not designed to evaluate long-term safety, and no functional outcome, including improved motor function, has been found.

In Study 1 Part 1, a double-blind, placebo-controlled dose-titration study, 12 DMD patients were randomized 2:1 to receive Vyondys 53 (golodirsen) or matching placebo. Those treated with Vyondys 53 (golodirsen) received four escalating dose levels via intravenous infusion, ranging from 4mg/kg/week to 30mg/kg/week for 2 weeks at each dose level.

The 12 DMD patients enrolled in Part 1 plus an additional 13 treatment-naïve patients with DMD amenable to exon 53 skipping continued in Study 1 Part 2, an open-label study assessing the efficacy and safety of Vyondys 53 (golodirsen) for 168 weeks at a dose of 30mg/kg/week. At study entry (either in Part 1 or Part 2), patients had a median age of 8 years and were on a stable dose of corticosteroids for at least 6 months. Efficacy was assessed based on change from baseline in the dystrophin protein level, a surrogate outcome measure. Mean dystrophin levels increased from 0.10% (SD 0.07) of normal at baseline to 1.02% (SD 1.03) of normal by week 48 of Part 2, with a mean change in dystrophin of 0.92% (SD 1.01) of normal levels ($p<0.001$); the median change from baseline was 0.88%.

As part of the FDA's accelerated approval of Vyondys 53 (golodirsen), a post-marketing confirmatory study titled ESSENCE is currently enrolling patients. It is a placebo-controlled study that must assess whether Vyondys 53 (golodirsen) improves motor function of DMD patients with a confirmed mutation of the dystrophin gene amenable to exon 53 skipping. It is expected to conclude by 2022. If a clinical benefit is not found, the FDA may withdraw approval.

There are two studies currently ongoing which are evaluating Vyondys 53 (golodirsen) in addition to the ESSENCE study. NCT04179409 is a phase 2, 48-week open-label extension study that is evaluating the safety and efficacy (as measured by change in dystrophin expression from baseline) of Vyondys 53 (golodirsen) in patients with a DMD gene that is amenable to exon 53 skipping after 1 year of treatment. It is expected to be completed by 2022. NCT03532542 is a phase 3, 148-week open-label extension study that is evaluating the safety and tolerability (as measured by the number of patients with serious adverse events [SAEs]) of Vyondys 53 (golodirsen) in patients with a DMD gene that is amenable to exon 53 skipping after receiving treatment for up to 144 weeks. It is expected to be completed by 2026.

In summary, the clinical benefit of treatment for DMD with Vyondys 53 (golodirsen) 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.

- J1429 - Injection, golodirsen, 10 mg (effective 7/1/20)

REFERENCES

- Vyondys 53 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; December 2019.
- FDA grants accelerated approval to first targeted treatment for rare Duchenne muscular dystrophy mutation. U.S. Food & Drug Administration. https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-first-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation. Accessed on December 19, 2019.
- Sarepta Therapeutics. A 48-Week, Open Label, Study to Evaluate the Efficacy and Safety of Casimersen, Eteplirsen, and Golodirsen in Subjects With Duchenne Muscular Dystrophy Carrying Eligible DMD Duplications. 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04179409?term=golodirsen&draw=1&rank=1.
- Sarepta Therapeutics. An Extension Study to Evaluate Casimersen or Golodirsen in Patients With Duchenne Muscular Dystrophy. 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT03532542?term=golodirsen&draw=1&rank=2.

POLICY HISTORY

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