

DRUG POLICY

Duvyzat® (givinostat)

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 medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

Duvyzat (givinostat) is a histone deacetylase (HDAC) inhibitor indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older. It is administered orally twice daily with food and may be used as monotherapy or in combination with corticosteroids.

This indication was approved by the Food and Drug Administration (FDA) in March 2024 based on the primary endpoint of the change from baseline at 72 weeks in the four-stair climb (4SC) in patients who were receiving stable doses of systemic corticosteroids.

POLICY

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

CLINICAL RATIONALE

Duvyzat (givinostat) is the first nonsteroidal drug approved for the treatment of all genetic variants of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older and is intended to be administered orally twice daily with food and may be used as monotherapy or in combination with corticosteroids. The precise mechanism by which DUVYZAT exerts its effect in patients with DMD is unknown.

Clinical Studies

The FDA approval of Duvyzat (givinostat) was based on efficacy data from a 72-week, phase III, randomized, double-blind, placebo-controlled multinational trial (EPIDYS) where participants were receiving stable doses of systemic corticosteroids. Participants were treated with oral givinostat twice daily (weight based) (n=118) or placebo (n=61). Participants were ambulant male patients between 6 and 17 years of age with genetically confirmed DMD.

The primary objective of the EPIDYS trial was to evaluate the change from baseline in the four-stair climb (4SC) test at 72 weeks in participants treated with Duvyzat or placebo. In the primary analysis, patients treated with Duvyzat showed statistically significant less decline in the 4SC compared to placebo (1.25 seconds vs. 3.03 seconds (difference -1.78 seconds); 95% CI -3.46 to -0.11; p = 0.037).

The secondary endpoints of the EPIDYS trial included the change from baseline in the North Star Ambulatory Assessment (NSAA) total score, time-to-rise from floor, and 6-minute walk test (6MWT). The results from the secondary endpoints were not statistically significant.

The most common adverse reactions (incidence $\geq 10\%$) in the clinical study were diarrhea (95%), abdominal pain (21%), thrombocytopenia (32%), nausea/vomiting (29%), hypertriglyceridemia (23%), and pyrexia (13%). The serious adverse reactions observed were hematological changes (dose-related thrombocytopenia and other signs of myelosuppression), increased triglycerides, gastrointestinal disturbances, and QTc prolongation. Patient's platelets and triglycerides should be monitored before initiation of Duvyzat. Duvyzat should not be initiated in patients with a platelet count less than $150 \times 10^9/L$.

In summary, the clinical benefit of treatment for DMD with Duvyzat (givinostat) has not been sufficiently demonstrated based on the currently available evidence. Ongoing, open-label extension studies are anticipated and may provide additional clinically meaningful endpoints and longer-term data to more clearly demonstrate maintenance of long-term motor function and mobility.

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.

REFERENCES

Duvyzat. Prescribing information. Italfarmaco S.A.; March 2024. Accessed March 21, 2024.

Mercuri E, Vilchez JJ, Boespflug-Tanguy O, et al. Safety and efficacy of givinostat in boys with Duchenne muscular dystrophy (EPIDYS): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol*. 2024;23:393-403. doi: 10.1016/S1474-4422(24)00036-X

National Institute of Health and Care Excellence (NICE). Givinostat for treating Duchenne muscular dystrophy in people 6 years and over. Last updated April 9, 2024c. Accessed April 16, 2024. <https://www.nice.org.uk/guidance/indevelopment/gid-ta11373>

POLICY HISTORY

Policy #: 05.05.55

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Revised:

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