Pharmacy Policy Bulletin: J-1387 Duvyzat (givinostat) – Commercial and Healthcare Reform	
Number: J-1387	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1387-002	**Original Date:** 06/05/2024
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Duvyzat (givinostat)
FDA-Approved Indication(s):	• Treatment of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older.

Background:	• Duvyzat is a histone deacetylase inhibitor (HDAC). Though the precise mechanism of action by which Duvyzat exerts its effect in DMD is unknown, it is thought to inhibit pathogenic downstream events of dystrophin deficiency (for example increased HDAC enzyme activity), thereby reducing inflammation and loss of muscle. • DMD is the most common type of muscular dystrophy, and is a genetic disorder characterized by progressive muscle degeneration and weakness. It is caused by a mutation in the *DMD* gene resulting in lack of functional dystrophin protein. DMD primarily affects boys and symptom onset is usually between the ages of 2 and 3. Symptoms progress from difficulty walking to impaired cardiac and respiratory function. Life expectancy may range from teens to early 30s. The estimated prevalence of DMD is 6 per 100,000 individuals in Europe and North America. • Genetic diagnosis of DMD is indicated in patients with an elevated creatinine kinase level. Diagnosis is confirmed if there is a pathogenic mutation in the dystrophin gene. • In Duvyzat's pivotal trial, EPIDYS, patients had a confirmed diagnosis of DMD, were ambulatory, and were required to be on a stable dose of corticosteroids for 6 months prior to enrollment. All patients continued to receive a standard-of-care steroid regimen throughout the study. • Prescribing Considerations: ○ Duvyzat has warnings and precautions for hematological changes, increased triglycerides, gastrointestinal disturbances, and QTc prolongation.

	○ Obtain and evaluate baseline platelet counts and triglycerides prior to initiation of Duvyzat. Do not initiate Duvyzat in patients with a platelet count of < 150 x 10^9/L. ○ Dosage modifications may be needed for decreased platelet counts, diarrhea, increased triglycerides, or QTc prolongation. ○ Closely monitor when Duvyzat is used in combination with an oral cytochrome P450 3A4 sensitive substrate or a sensitive substrate of the organic cation transporter 2, for which small change in substrate plasma concentration may lead to serious toxicities. ○ Avoid concomitant use with other drugs that prolong the QTc interval; monitor electrocardiogram if concomitant use cannot be avoided. ○ Duvyzat is supplied in bottles containing 140 mL oral suspension. Each mL contains 8.86 mg of Duvyzat. Discard any unused medication remaining after 60 days of first opening the bottle.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Duvyzat may be approved when all of the following criteria are met **(A. through E.)**:

- **A.** The member is 6 years of age or older.
- **B.** The member has a diagnosis of Duchenne muscular dystrophy (ICD-10: G71.01), confirmed by a documented pathogenic mutation in the dystrophin gene.
- **C.** The member is ambulatory.
- **D.** The medication is prescribed by or in consultation with a physician who specializes in treating neuromuscular disorders (for example neurologist).
- **E.** The member meets one (1) of the following **(1. or 2.)**:
  - **1.** The member meets both of the following **(a. and b.)**:
    - **a.** The member has been stable on corticosteroid therapy for at least 6 months.
    - **b.** The member will be using Duvyzat in combination with corticosteroid therapy.
  - **2.** The member has experienced contraindication or intolerance to corticosteroid therapy.

II. Reauthorization

When a benefit, reauthorization of Duvyzat may be approved when all the following criteria are met **(A., B., and C.)**:

- **A.** The prescriber attests that the member has experienced a positive clinical response to therapy.
- **B.** The member continues to be ambulatory.
- **C.** The member meets one (1) of the following **(1. or 2.)**:
  - **1.** The member meets both of the following **(a. and b)**:
    - **a.** The member has been stable on corticosteroid therapy for at least 6 months.
    - **b.** The member will continue to use Duvyzat in combination with corticosteroid therapy.
  - **2.** The member has experienced contraindication or intolerance to corticosteroid therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Duvyzat [package insert]. Concord, MA: ITF Therapeutics, LLC; March 2024.
2. Muscular Dystrophy Association. Duchenne Muscular Dystrophy (DMD). Available at: https://www.mda.org/disease/duchenne-muscular-dystrophy. Accessed April 09, 2025.
3. U.S. Food & Drug Administration. FDA Approves Nonsteroidal Treatment for Duchenne Muscular Dystrophy. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-nonsteroidal-treatment-duchenne-muscular-dystrophy. Accessed April 09, 2025.
4. Muscular Dystrophy News. FDA approves oral givinostat, as Duvyzat, to treat Duchenne MD. Available at: https://musculardystrophynews.com/news/fda-approves-oral-givinostat-now-duvyzat-treat-duchenne-md/. Accessed April 09, 2025.
5. 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(4): 393-403.