Clinical Policy: Givinostat (Duvyzat)

Reference Number: CP.PHAR.644
Effective Date: 03.21.24
Last Review Date: 08.24
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Givinostat (Duvyzat™) is a histone deacetylase inhibitor.

FDA Approved Indication(s)

Duvyzat is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Duvyzat is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Duchenne Muscular Dystrophy (must meet all)**:**

1. Diagnosis of DMD confirmed by one of the following (a or b):
   a. Genetic testing (e.g., dystrophin deletion or duplication mutation found);
   b. If genetic studies are negative (i.e., no mutation identified), positive muscle biopsy (e.g., absence of dystrophin protein);
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 6 years;
4. Member is ambulatory (e.g., ability to walk with or without assistive devices, not wheelchair dependent);
5. Documentation of member's baseline ambulatory function as evidenced by one of the following motor function tests (a, b, c, d, e, or f):
   a. North Star Ambulatory Assessment (NSAA);
   b. 10-meter (10m) timed test;
   c. 100-meter (100m) timed test;
   d. Time to ascend 4 steps;
   e. Time to rise from the floor (TRF);
   f. 6-minute walk test (6MWT);
6. Documentation of a recent (within the last 30 days) platelet count ≥ 150 x 10^9/L;
7. Member has been on a stable dose of an oral corticosteroid (e.g., prednisone, Emflaza®*, Agamree®*) for ≥ 6 months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for Emflaza and Agamree*

8. Duvyzat is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
9. Documentation of member's body weight in kg;
10. Dose does not exceed 106.4 mg (12 mL) per day (*see Section V for weight-based dosing*).

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Duchenne Muscular Dystrophy (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement or stabilization in member's ambulatory function from baseline in any of the following motor function tests: NSAA, 10m or 100m timed test, time to ascend 4 steps, TRF, 6MWT;
3. Member has been assessed by a neurologist within the last 6 months;
4. Duvyzat is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
5. Documentation of member's body weight in kg;
6. If request is for a dose increase, new dose does not exceed 106.4 mg (12 mL) per day (*see Section V for weight-based dosing*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6MWT: 6-minute walk test
AAN: American Academy of Neurology
FDA: Food and Drug Administration
m: meter
NSAA: North Star Ambulatory Assessment
TRF: time to rise from the floor

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Corticosteroids are routinely used in DMD management with established efficacy in slowing decline of muscle strength and function (including motor, respiratory, and cardiac). They are recommended for all DMD patients per the American Academy of Neurology (AAN) and DMD Care Considerations Working Group; in addition, the AAN guidelines have been endorsed by the American Academy of Pediatrics, the American Association of Neuromuscular & Electrodiagnostic Medicine, and the Child Neurology Society.
  - The DMD Care Considerations Working Group guidelines, which were updated in 2018, continue to recommend corticosteroids as the mainstay of therapy.

- Prednisone is the corticosteroid with the most available evidence. A second corticosteroid commonly used is Emflaza (deflazacort), which was FDA approved for DMD in February 2017. On October 2023, a third corticosteroid, Agamree (vamorolone), was approved by the FDA for DMD.

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>DMD</td><td>Administered orally twice daily with food according to actual body weight:
<table>
<tr><th>Actual Body Weight</th><th>Dose (mg)</th><th>Dose (mL)</th></tr>
<tr><td>≥ 10 kg and < 20 kg</td><td>22.2 mg</td><td>2.5 mL</td></tr>
<tr><td>≥ 20 kg and < 40 kg</td><td>31 mg</td><td>3.5 mL</td></tr>
<tr><td>≥ 40 kg and < 60 kg</td><td>44.3 mg</td><td>5 mL</td></tr>
<tr><td>60 kg or more</td><td>53.2 mg</td><td>6 mL</td></tr>
</table>
Dose modification may be needed for decreased platelet counts, diarrhea, increased triglycerides, or QTc prolongation</td><td>106.4 mg (12 mL) per day</td></tr>
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VI. Product Availability

Oral suspension: 8.86 mg/mL

VII. References

1. Duvyzat Prescribing Information. Concord, MA: ITF Therapeutics, LLC.; March 2024. Available at: https://www.duvyzat.com/PI. Accessed March 27, 2024.
2. ClinicalTrials.gov. Clinical study to evaluate the efficacy and safety of givinostat in ambulant patients with Duchenne muscular dystrophy. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT02851797. Accessed March 27, 2024.
3. Mercuri E, Vilchez JJ, Boespflug-Tanguy O et al. Safety and efficacy of givinostat in boys with Duchenne muscular dystrophy (EPIDYS): a multicentre, randomized, double-blind, placebo-controlled, phase 3 trial. The Lancet Neurology April 2024;23(4):393-403.
4. Gloss D, Moxley RT, Ashwal S, Oskoui M. Practice guideline update summary: corticosteroid treatment of Duchenne muscular dystrophy. Report of the guideline development subcommittee of the American Academy of Neurology. Neurology. 2016; 86:465-472. Reaffirmed January 22, 2022.
5. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	08.15.23	11.23
RT4: Duvyzat is now FDA approved – criteria updated per FDA labeling: added option for positive muscle biopsy for diagnosis of DMD if genetic studies negative per DMD Care Considerations	05.07.24	08.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Working Group; removed age restriction of < 18 years at therapy initiation; revised ambulatory criteria with removal of 4SC ≤ 8 seconds requirement; removed QTcF, triglycerides and LVEF contraindications from criteria; added documentation of member's baseline ambulatory function as evidenced by motor function tests; for continued therapy, added improvement or stabilization in member's ambulatory function from baseline as example of responding positively to therapy; references reviewed and updated.		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.