BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.21.248

| | | | |
|---|---|---|---|
| **Section:** | Prescription Drugs | **Effective Date:** | January 1, 2026 |
| **Subsection:** | Antineoplastic Agents | **Original Policy Date:** | September 5, 2025 |
| **Subject:** | Modeyso | **Page:** | 1 of 4 |

***Last Review Date:*** December 12, 2025

# Modeyso

## Description

### Modeyso (dordaviprone)

**Background**
Modeyso (dordaviprone) is a protease activator of the mitochondrial caseinolytic protease P (ClpP). Modeyso also inhibits the dopamine D2 receptor. Diffuse midline gliomas harboring an H3 K27M mutation are associated with the loss of H3 K27 trimethylation. In-vitro Modeyso activated the integrated stress response, induced apoptosis, and altered mitochondrial metabolism leading to restored histone H3 K27 trimethylation in H3 K27M-mutant diffuse glioma models (1).

**Regulatory Status**
FDA-approved indications: Modeyso is a protease activator indicated for the treatment of adult and pediatric patients 1 year of age and older with diffuse midline glioma harboring an H3 K27M mutation with progressive disease following prior therapy (1).

Treatment with Modeyso has been associated with hypersensitivity and QTc interval prolongation. Discontinue if the patient shows signs of hypersensitivity, anaphylaxis, or QT prolongation, and initiate appropriate medical treatment and supportive care (1).

Modeyso may cause fetal harm when administered to a pregnant woman. Advise female patients of reproductive potential to use effective contraception during treatment with Modeyso and for 1 month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Modeyso and for 1 month after the last dose (1).

The safety and effectiveness of Modeyso in pediatric patients less than 1 year of age have not been established (1).

**Related Policies**

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Modeyso may be considered **medically necessary** if the conditions indicated below are met.

Modeyso may be considered **investigational** for all other indications.

## Prior-Approval Requirements

**Age** 1 year of age or older

**Diagnosis**

Patient must have the following:

1. Diffuse midline glioma
    a. Tumor carries a H3 K27M mutation
    b. Patient has progressive disease following prior therapy

**AND ALL** of the following:

1. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Modeyso and for 1 month after the last dose
2. Male patients with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Modeyso and for 1 month after the last dose

## Prior – Approval *Renewal* Requirements

**Age** 1 year of age or older

**Diagnosis**

Patient must have the following:

1. Diffuse midline glioma

**AND ALL** of the following:

1. **NO** disease progression or unacceptable toxicity
2. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Modeyso and for 1 month after the last dose
3. Male patients with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Modeyso and for 1 month after the last dose

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Quantity** 60 capsules per 84 days

**Duration** 12 months

### Prior – Approval *Renewal* Limits

Same as above

## Rationale

**Summary**

Modeyso (dordaviprone) is indicated for the treatment of diffuse midline glioma. Modeyso has warnings for hypersensitivity, QTc interval prolongation, and embryo-fetal toxicity. The safety and effectiveness of Modeyso for pediatric patients less than 1 year of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Modeyso while maintaining optimal therapeutic outcomes.

**References**

1. Modeyso [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; August 2025.
2. NCCN Drugs & Biologics Compendium® Dordaviprone 2025. National Comprehensive Cancer Network, Inc. Accessed on November 3, 2025.

## Policy History

| Date | Action |
|---|---|
| September 2025 | Addition to PA |
| December 2025 | Annual review and reference update |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.**