# Modeyso™ (dordaviprone) Included in National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology for H3 K27M-mutant Diffuse Glioma

September 09, 2025

*Modeyso, the first treatment option for this ultra-rare and aggressive brain tumor, is commercially available in the United States*

*For U.S. media and investors only*

DUBLIN, Sept. 9, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that Modeyso™ (dordaviprone) is recommended by the National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a category 2A single-agent treatment option for pediatric and adult patients with recurrent or progressive diffuse high-grade glioma harboring an H3 K27M mutation.

*Modeyso* was granted accelerated approval by the U.S. Food and Drug Administration (FDA) on August 6, 2025 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] Continued approval for this indication may be contingent upon verification and description of clinical benefit in the Phase 3 ACTION confirmatory trial.[1]

"The rapid addition of *Modeyso* to the NCCN Guidelines® – in both the Pediatric Central Nervous System Cancers and Central Nervous System Cancers guidelines – reflects the urgency of the unmet need that patients are faced with when diagnosed with this devastating and aggressive brain tumor," said Kelvin Tan, MB BCh, MRCPCH, chief medical affairs officer of Jazz Pharmaceuticals. "We are proud to bring *Modeyso* to patients in the U.S. as the first treatment option for recurrent H3 K27M-mutant diffuse midline glioma, representing a meaningful shift in the treatment landscape for patients and their families."

The NCCN Guidelines® play a pivotal role in decision-making processes for individuals involved in cancer care all over the world, including physicians, nurses, pharmacists, payers, and patients and their families. The guidelines present expert recommendations for cancer screening, diagnosis and treatment, as well as cancer care options, and are utilized in cancer treatment decision-making to drive positive patient outcomes. NCCN is a not-for-profit alliance of 33 leading cancer centers devoted to patient care, research and education. NCCN is dedicated to defining and advancing effective, equitable, accessible and quality cancer care and prevention so all people can live better lives. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The FDA approval of *Modeyso* was based on an integrated efficacy analysis of 50 patients with recurrent H3 K27M-mutant diffuse midline glioma, selected from five open-label clinical studies based on pre-specified eligibility criteria. The overall response rate (ORR), as assessed by blinded independent central review (BICR) using Response Assessment in Neuro-Oncology (RANO) 2.0 criteria, was 22% (95% CI: 12 to 36), with an additional responder identified by integrated RANO 2.0. Among responders, the median duration of response was 10.3 months (95% CI: 7.3 to 15.2), with 73% maintaining their response for at least six months and 27% for at least 12 months.[1]

The safety of *Modeyso* was evaluated in 376 adult and pediatric patients with glioma across four open-label clinical studies. Serious adverse reactions occurred in 33% of patients. Serious adverse reactions reported in more than 2% of patients included hydrocephalus (5%), vomiting (4.3%), headache (3.2%), seizure (2.4%) and muscular weakness (2.1%). The most common adverse reactions in patients who received *Modeyso* (≥20%) were fatigue, headache, vomiting, nausea and musculoskeletal pain.[1] See additional safety information below and full prescribing information: https://pp.jazzpharma.com/pi/modeyso.en.USPI.pdf

**About H3 K27M-Mutant Diffuse Midline Glioma**
H3 K27M-mutant diffuse midline glioma is a rare and highly aggressive brain tumor that primarily affects the midline structures of the brain and spinal cord.[2,3] It is characterized by a specific genetic mutation (H3 K27M) that disrupts epigenetic regulation and drives tumor growth.[4] Most commonly diagnosed in children and young adults, patients with this type of glioma often face an extremely poor prognosis, with limited therapeutic options and very low survival rates following recurrence.[5] Median survival is approximately one year from diagnosis and less than six months after disease progression following frontline therapy.[5]

**About Modeyso™ (dordaviprone)**
*Modeyso* (dordaviprone) is approved by the U.S. Food and Drug Administration (FDA) 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] *Modeyso* is an orally administered small molecule given once weekly. *Modeyso* is a protease activator of the mitochondrial caseinolytic protease P (ClpP) and also inhibits dopamine D2 receptor (DRD2). In vitro, dordaviprone activates the integrated stress response, induces apoptosis and alters mitochondrial metabolism, leading to restored histone H3 K27 trimethylation in H3 K27M-mutant diffuse glioma.[1]

*Modeyso* received accelerated approval based on a pre-specified integrated efficacy analysis of 50 adult and pediatric patients with recurrent H3 K27M-mutant diffuse midline glioma enrolled across five open-label clinical studies (ONC006, ONC013, ONC014, ONC016 and ONC018). Continued approval may be contingent upon verification and description of clinical benefit in the ongoing Phase 3 ACTION trial (NCT05580562), which is evaluating the safety and clinical benefit of *Modeyso* in newly diagnosed patients with H3 K27M-mutant diffuse glioma following radiotherapy.[4] *Modeyso* was developed by Chimerix prior to its acquisition by Jazz Pharmaceuticals in April 2025.

*Modeyso* (dordaviprone) is not approved anywhere else in the world.

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS**

*Hypersensitivity*
MODEYSO can cause severe hypersensitivity reactions.

In the pooled safety population, Grade 3 hypersensitivity reactions occurred in 0.3% of patients receiving MODEYSO. Signs and symptoms of hypersensitivity may include rash, hives, fever, low blood pressure, wheezing, or swelling of the face or throat.

Inform patients about the signs and symptoms of hypersensitivity reactions and instruct them to seek immediate medical attention if symptoms occur.

If clinically significant hypersensitivity or anaphylaxis occur, immediately interrupt MODEYSO and initiate appropriate medical treatment and supportive care. Based on the severity of the adverse reaction, temporarily interrupt or permanently discontinue MODEYSO.

*QTc Interval Prolongation*
MODEYSO causes concentration-dependent QTc interval prolongation, which can increase the risk for ventricular tachyarrhythmias (e.g. torsades de pointes) or sudden death.

In patients who received MODEYSO and underwent at least one post baseline ECG, QTcF increase of >60 msec compared to baseline and QTcF >500 msec occurred in 6% and 1.2% of patients, respectively.

Monitor ECGs and electrolytes prior to initiation and periodically during treatment, as clinically indicated. Increase the frequency of monitoring in patients with congenital long QT syndrome, existing QTc prolongation, a history of ventricular arrhythmias, electrolyte abnormalities, heart failure, or who are taking strong or moderate CYP3A4 inhibitors.

Avoid concomitant use with other agents known to prolong the QT interval. If concomitant use cannot be avoided, increase the frequency of monitoring and separate administration of MODEYSO and QT-prolonging product.

Interrupt or reduce the dose of MODEYSO in patients who develop QT prolongation; permanently discontinue in patients with signs of life-threatening arrhythmias.

*Embryo-Fetal Toxicity*
MODEYSO can cause fetal harm when administered to a pregnant woman.
Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females 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

**ADVERSE REACTIONS**
Serious adverse reactions occurred in 33% of the 376 patients who received MODEYSO. Serious adverse reactions in >2% of patients included hydrocephalus (5%), vomiting (4.3%), headache (3.2%), seizure (2.4%), and muscular weakness (2.1%). Fatal adverse reactions occurred in 1% of patients who received MODEYSO, including cardiac arrest (0.5%), intracranial hemorrhage (0.3%), and encephalopathy (0.3%).

The most common adverse reactions (≥20%) reported in clinical trials with MODEYSO were fatigue (34%), headache (32%), vomiting (24%), nausea (24%), and musculoskeletal pain (20%). The most common (≥2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes (7%), decreased calcium (2.7%), and increased alanine aminotransferase (2.4%).

**DRUG INTERACTIONS**
*Strong and Moderate CYP3A4 Inhibitors*
Avoid concomitant use of MODEYSO with strong and moderate CYP3A4 inhibitors. If concomitant use cannot be avoided, reduce the MODEYSO dose as recommended and monitor for toxicity.

*Strong and Moderate CYP3A4 Inducers*
Avoid concomitant use of strong and moderate CYP3A4 inducers with MODEYSO.

**USE IN SPECIFIC POPULATIONS**
*Lactation*
There are no data on the presence of MODEYSO in human milk because of the potential for serious adverse reactions from MODEYSO in breastfed children, advise women not to breastfeed during treatment with MODEYSO and for 1 week after the last dose.

*Pediatric Use*
The safety and effectiveness of MODEYSO have not been established in patients less than 1 year of age. Dosing has not been established for patients weighing less than 22 pounds (10 kg).

Please refer to the full Prescribing Information, including both Patient Information and Instructions for Use, for complete safety and administration information.

**About Jazz Pharmaceuticals**
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharma company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing potentially life-changing medicines for people with serious diseases – often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience. Jazz is headquartered in Dublin, Ireland with research and development laboratories, manufacturing facilities and employees in multiple countries committed to serving patients worldwide. Please visit www.jazzpharmaceuticals.com for more information.

**Contacts:**
**Media:**
Kristin Bhavnani
Head of Global Corporate Communications

Jazz Pharmaceuticals plc
**CorporateAffairsMediaInfo@jazzpharma.com**
Ireland +353 1 637 2141
U.S. +1 215 867 4948

**Investors:**
Jack Spinks
Executive Director, Investor Relations
Jazz Pharmaceuticals plc
**investorinfo@jazzpharma.com**
Ireland +353 1 634 3211
U.S. +1 650 496 2717

[1] MODEYSO (dordaviprone) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

[2] Yang, Z., Sun, L., Chen, et al. New progress in the treatment of diffuse midline glioma with H3K27M alteration. Heliyon. 2024;10(2).

[3] National Cancer Institute. Diffuse Midline Glioma: Diagnosis and Treatment. Updated August 20, 2024. Accessed September 8, 2025. https://www.cancer.gov/rare-brain-spine-tumor/tumors/diffuse-midline-gliomas

[4] ClinicalTrials.gov. ONC201 in H3 K27M-mutant Diffuse Glioma Following Radiotherapy (the ACTION Study) (ACTION). Updated August 26, 2025. Accessed September 8, 2025. Study Details | ONC201 in H3 K27M-mutant Diffuse Glioma Following Radiotherapy (the ACTION Study) | ClinicalTrials.gov

[5] Bagley, S. J., Umemura, et al. Prognostic Features of Recurrent Midline and H3 K27M-Mutant Glioma. *Cancers*. 2025;17(13):2107. https://doi.org/10.3390/cancers17132107

View original content to download multimedia:https://www.prnewswire.com/news-releases/modeyso-dordaviprone-included-in-national-comprehensive-cancer-network-nccn-clinical-practice-guidelines-in-oncology-for-h3-k27m-mutant-diffuse-glioma-302549794.html

SOURCE Jazz Pharmaceuticals plc