

MODEYSO- dordaviprone capsule

Jazz Pharmaceuticals, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MODEYSO safely and effectively. See full prescribing information for MODEYSO.

MODEYSO™ (dordaviprone) capsules, for oral use
Initial U.S. Approval: 2025

INDICATIONS AND USAGE

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)

This indication is approved under accelerated approval based on response rate and duration of response [see *Clinical Studies* (14)]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

DOSAGE AND ADMINISTRATION

- Select patients for treatment with MODEYSO based on the presence of an H3 K27M mutation from tumor specimens. (2.1)
- Monitor ECG and electrolytes before starting MODEYSO and periodically during treatment as clinically indicated. (2.2)
- The recommended dose in adult patients is 625 mg orally once weekly. (2.3)
- The recommended dose in pediatric patients weighing ≥ 10 kg is based on body weight (see Table 1). (2.3)
- Take MODEYSO orally once weekly on an empty stomach (at least 1 hour before or 3 hours after food intake). (2.3)
- Continue MODEYSO until disease progression or unacceptable toxicity. (2.3)

DOSAGE FORMS AND STRENGTHS

- Capsules: 125 mg (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity: If clinically significant hypersensitivity or anaphylaxis occur, immediately discontinue MODEYSO and initiate appropriate medical treatment and supportive care. (5.1)
- QTc Interval Prolongation: MODEYSO causes concentration dependent QTc interval prolongation. Interrupt or reduce the dose of MODEYSO in patients who develop QT prolongation, and permanently discontinue MODEYSO in patients with signs of life-threatening arrhythmias. (5.2, 12.2)
- Embryo-fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception. (5.3, 8.1, 8.3)

ADVERSE REACTIONS

The most common ($\geq 20\%$) adverse reactions are fatigue, headache, vomiting, nausea, and musculoskeletal pain. The most common ($\geq 2\%$) Grade 3 or 4 laboratory abnormalities are decreased lymphocytes, decreased calcium, and increased alanine aminotransferase. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Chimerix at toll-free phone # 1-866-662-2679 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- CYP3A4 Inhibitors: Avoid concomitant use of strong and moderate CYP3A4 inhibitors with MODEYSO. If concomitant use cannot be avoided for adults and pediatric patients who weigh at least 52.5 kg, reduce the dose of MODEYSO as recommended. (2.5, 7.1)
- CYP3A4 Inducers: Avoid concomitant use of strong and moderate CYP3A4 inducers with MODEYSO. (7.1)
- Drugs Known to Prolong QTc Interval: Avoid concomitant use of MODEYSO with products known to

prolong the QTc interval. If concomitant use cannot be avoided, separate administration of MODEYSO and the QT-prolonging product. (5.2, 7.2, 12.2)

-----USE IN SPECIFIC POPULATIONS-----

- Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 8/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Patient Selection
- 2.2 Recommended Testing Before Starting MODEYSO
- 2.3 Recommended Dosage and Administration
- 2.4 Dosage Modifications for Adverse Reactions
- 2.5 Dosage Modifications for CYP3A4 Inhibitors

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Hypersensitivity
- 5.2 QTc Interval Prolongation
- 5.3 Embryo-fetal Toxicity

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience

7 DRUG INTERACTIONS

- 7.1 Effect of Other Drugs on MODEYSO
- 7.2 Drugs Known to Prolong QTc Interval

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation
- 8.3 Females and Males of Reproductive Potential
- 8.4 Pediatric Use
- 8.5 Geriatric Use

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

MODEYSO is 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.

This indication is approved under accelerated approval based on overall response rate and duration of response [see *Clinical Studies (14)*]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for treatment with MODEYSO based on the presence of an H3 K27M mutation from tumor specimens [see *Clinical Studies (14)*]. An FDA-approved test for the detection of this mutation is not currently available.

2.2 Recommended Testing Before Starting MODEYSO

Monitor electrocardiograms (ECG) and electrolytes before starting MODEYSO and periodically during treatment as clinically indicated [see *Warnings and Precautions (5.2)* and *Drug Interactions (7.2)*].

2.3 Recommended Dosage and Administration

Take MODEYSO on an empty stomach (at least 1 hour before or 3 hours after food intake) [see *Clinical Pharmacology (12.3)*].

Adults

The recommended dosage of MODEYSO is 625 mg orally once weekly.

Pediatrics

The recommended dosage of MODEYSO in pediatric patients aged 1 to <17 years who weigh at least 10 kg is based on body weight (Table 1). A recommended dosage of MODEYSO has not been established in pediatric patients who weigh less than 10 kg.

Table 1: Recommended Body Weight-Based Dosage for Pediatric Patients

Body Weight (kg)	Recommended Dosage
10 kg to <12.5 kg	125 mg Once Weekly
12.5 kg to <27.5 kg	250 mg Once Weekly
27.5 kg to <42.5 kg	375 mg Once Weekly
42.5 kg to <52.5 kg	500 mg Once Weekly

≥52.5 kg

625 mg Once Weekly

Continue MODEYSO until disease progression or unacceptable toxicity.

Swallow capsules whole. For patients unable to swallow capsules whole, open each capsule, mix contents with approximately 15 to 30 mL of liquid (sports drink, apple juice, lemonade, or water) before administration, and administer orally as a liquid [see *Patient Counseling Information (17)*]. Once mixed, administer within 2 hours of preparation, or discard and mix a new dose.

Vomiting

If vomiting occurs after taking a dose, do not take an additional dose and take the next dose at the regularly scheduled time.

Missed Dose

If a dose is missed within 2 days, take the missed dose as soon as possible. If a dose is missed by more than 2 days, skip the missed dose and take the next dose at the scheduled time.

2.4 Dosage Modifications for Adverse Reactions

The recommended dosage reductions for adverse reactions for MODEYSO are provided in Table 2.

Table 2: Recommended Dosage Reductions for Adverse Reactions

Patient's Weight (kg)	First Dosage Reduction	Second Dosage Reduction
Pediatric patients 10 kg to <12.5 kg	Permanently discontinue	N/A
Pediatric patients 12.5 kg to <27.5 kg	125 mg once weekly	Permanently discontinue
Pediatric patients 27.5 kg to <42.5 kg	250 mg once weekly	125 mg once weekly
Pediatric patients 42.5 kg to <52.5 kg	375 mg once weekly	250 mg once weekly
Pediatric patients ≥52.5 kg and adult patients	500 mg once weekly	375 mg once weekly

The recommended dosage modifications for adverse reactions are provided in Table 3.

Table 3: Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity ^a	Dosage Modification ^b
Hypersensitivity [see <i>Warnings and Precautions (5.1)</i>]	Any grade	If hypersensitivity is suspected based on clinical judgement, interrupt MODEYSO until resolution of the event. Permanently discontinue MODEYSO in patients who develop serious

		hypersensitivity reactions.
QTc Interval Prolongation [see Warnings and Precautions (5.2)]	QTc absolute value >500 ms or An increase of >60 ms from baseline	Interrupt MODEYSO until QTc interval \leq 480 ms or return to baseline. Resume MODEYSO at the next lower dose level.
	Torsades de pointes, polymorphic ventricular tachycardia or signs or symptoms of serious or life-threatening arrhythmia	Permanently discontinue MODEYSO.
Other Adverse Reactions [see Adverse Reactions (6.1)]	Grade 3 or 4	Interrupt MODEYSO until \leq Grade 1 or return to baseline. Resume MODEYSO at the next lower dose level.
	Recurrent Grade 4	Permanently discontinue MODEYSO.

a. National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

b. See Table 2 for recommended dosage reductions.

2.5 Dosage Modifications for CYP3A4 Inhibitors

Avoid concomitant use of strong and moderate CYP3A4 inhibitors with MODEYSO.

- If concomitant use of a strong CYP3A4 inhibitor cannot be avoided for adult and pediatric patients who weigh at least 52.5 kg, reduce the dose of MODEYSO from 625 mg to 375 mg once weekly.
- If concomitant use of a moderate CYP3A4 inhibitor cannot be avoided for adult and pediatric patients who weigh at least 52.5 kg, reduce the dose of MODEYSO from 625 mg to 500 mg once weekly.
- The recommended dosage for pediatric patients weighing less than 52.5 kg who are receiving strong or moderate CYP3A4 inhibitors has not been established.

Upon discontinuation of the CYP3A4 inhibitor, wait for 3 to 5 plasma half-lives of the CYP3A4 inhibitor, then increase MODEYSO to the dose that was taken before starting the CYP3A4 inhibitor [see Drug Interactions (7.1) and Clinical Pharmacology (12.3)].

3 DOSAGE FORMS AND STRENGTHS

Capsules: 125 mg, white, opaque, hard capsules printed with “DDP” and “125” on the body and “CMRX” on the cap of the capsule. Each capsule contains 125 mg dordaviprone.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

MODEYSO can cause severe hypersensitivity reactions.

In the pooled safety population [see *Adverse Reactions (6.1)*], 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 [see *Dosage and Administration (2.4)*].

5.2 QTc Interval Prolongation

MODEYSO causes a concentration-dependent QTc interval prolongation [see *Clinical Pharmacology (12.2)*], which can increase the risk for ventricular tachyarrhythmias (e.g., torsades de pointes) or sudden death.

In the pooled safety population [see *Adverse Reactions (6.1)*], of the 82 patients who underwent at least one post-baseline ECG assessment, 6% experienced an increase in QTc of >60 msec compared to baseline after receiving MODEYSO and 1.2% had an increase in QTc to >500 msec.

Monitor ECGs and electrolytes prior to starting MODEYSO and then periodically during treatment as clinically indicated.

Significant prolongation of the QT interval may occur when MODEYSO is taken concomitantly with other products that have a known potential to prolong the QT interval. Avoid concomitant use of MODEYSO with products known to prolong the QT interval. If concomitant use cannot be avoided, separate administration of MODEYSO and the QT-prolonging product [see *Drug Interactions (7.2)* and *Clinical Pharmacology (12.2)*].

Increase the frequency of monitoring when administering MODEYSO to patients taking other products that have a known potential to prolong the QT interval and 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. Interrupt or reduce the dose of MODEYSO in patients who develop QT prolongation, and permanently discontinue MODEYSO in patients with signs of life-threatening arrhythmias [see *Dosage and Administration (2.4)*].

5.3 Embryo-fetal Toxicity

Based on findings from animal studies and its mechanism of action, MODEYSO can cause fetal harm when administered to a pregnant woman. In embryo-fetal development studies, oral administration of dordaviprone to pregnant rats and rabbits during

organogenesis caused embryo-fetal mortality, alterations to growth, and structural abnormalities at exposures below the human exposure at the highest recommended dose.

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 [*see Use in Specific Populations (8.1, 8.3)*].

6 ADVERSE REACTIONS

The following potential clinically significant adverse reactions are described elsewhere in the labelling:

- Hypersensitivity [*see Warnings and Precautions (5.1)*].
- QTc Interval Prolongation [*see Warnings and Precautions (5.2)*].

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The pooled safety population described in WARNINGS AND PRECAUTIONS and below reflects exposure to MODEYSO at the recommended weight-based dose taken until disease progression or unacceptable toxicity in 376 adult and pediatric patients with glioma across four open-label clinical studies (ONC006, ONC013, ONC014, and ONC018) [*see Clinical Studies (14)*].

Of the 376 patients who received MODEYSO, 35% were exposed for 6 months, and 17% were exposed for 1 year.

The median age was 23 years (range: 3 to 80): 30% were 2 to 11 years old, 11% were 12 to 17 years old, 55% were 18 to 64 years old, and 3.7% were 65 years or older. Fifty-two percent (52%) were female; 74% White, 10% unknown race or race not reported, 9% Black or African American, 4% Asian, 2.9% other or multiple races; and 13% were of Hispanic or Latino ethnicity. Karnofsky/Lansky Performance Status (KPS/LPS) score was 80 to 100 in 66% of patients, 60 to 70 in 27%, and <60 in 7%.

Relevant disease characteristics included primary tumor locations in the midline (91%) and non-midline regions (9%); 33% had diffuse intrinsic pontine glioma (DIPG); 30% had multifocal disease; 79% had an H3 K27M mutation; 75% had recurrent disease.

Serious adverse reactions occurred in 33% of 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%).

Permanent discontinuation of MODEYSO due to an adverse reaction occurred in 2.1% of patients. Adverse reactions which resulted in permanent discontinuation of MODEYSO in >1 patient included confusional state.

Dosage interruptions of MODEYSO due to an adverse reaction occurred in 6% of patients. Adverse reactions which required dosage interruption in >1 patient included increased alanine aminotransferase, increased aspartate aminotransferase, decreased lymphocyte count, muscular weakness, and aspiration pneumonia.

Dose reductions of MODEYSO due to an adverse reaction occurred in 2.7% of patients. Adverse reactions which required dose reductions in >1 patient included decreased neutrophil count and increased alanine aminotransferase.

The most common adverse reactions ($\geq 20\%$) were fatigue, headache, vomiting, nausea, and musculoskeletal pain. The most common ($\geq 2\%$) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes, decreased calcium, and increased alanine aminotransferase.

Adverse reactions that occurred in at least 10% of patients treated with MODEYSO are presented in Table 4.

Table 4: Adverse Reactions ($\geq 10\%$) in Patients with Glioma Who Received MODEYSO in ONC006, ONC013, ONC014, and ONC018

Adverse Reaction	MODEYSO (N=376)	
	All Grades (%)	Grade 3 or 4 (%)
General Disorders		
Fatigue ^a	34	3.2
Gait disturbance	16	3.7
Nervous System Disorders		
Headache ^b	32	4.3
Cranial nerve disorders ^c	16	1.3
Hemiparesis	15	4.5
Dysarthria	13	2.7
Dizziness	13	0.5
Ataxia	10	1.3
Gastrointestinal Disorders		
Vomiting	24	2.7
Nausea	24	0.8
Dysphagia	13	2.1
Constipation	11	0
Musculoskeletal and Connective Tissue Disorders		
Musculoskeletal pain ^d	20	2.9
Muscular weakness	13	4.5
Metabolism and Nutrition Disorders		
Hyperglycemia	12	0.8
Infections and Infestations		
Rash ^e	11	0.8

^a. Includes asthenia.

- b. Includes head discomfort and sinus headache.
- c. Includes accessory nerve disorder, auditory nerve disorder, facial nerve disorder, facial paralysis, facial paresis, glossopharyngeal nerve disorder, hypoglossal nerve disorder, IIIrd nerve disorder, IIIrd nerve paralysis, IVth nerve disorder, IVth nerve paralysis, tongue paralysis, trigeminal nerve disorder, trigeminal neuralgia, VIth nerve disorder, VIth nerve paralysis, and VIth nerve paresis.
- d. Includes back pain, pain in extremity, arthralgia, neck pain, non-cardiac chest pain, myalgia, bone pain, musculoskeletal chest pain, musculoskeletal stiffness, and spinal pain.
- e. Includes dermatitis, dermatitis acneiform, dermatitis bullous, eczema, erythema multiforme, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, and rash pustular.

Other clinically important adverse reactions observed in less than 10% of patients treated with MODEYSO were peripheral neuropathy, seizure, diarrhea, tremor, and venous thromboembolic events.

Selected laboratory abnormalities that occurred in at least 10% of patients treated with MODEYSO are presented in Table 5.

Table 5: Select Laboratory Abnormalities ($\geq 10\%$) that Worsened from Baseline in Patients with Glioma Receiving MODEYSO in ONC006, ONC013, ONC014, and ONC018

Laboratory Abnormality^a	MODEYSO^b	
	All Grades (%)	Grade 3 or 4 (%)
Chemistry		
Alanine aminotransferase increased	28	2.4
Aspartate aminotransferase increased	22	0.9
Calcium decreased	20	2.7
Sodium decreased	14	0.3
Potassium decreased	13	0.3
Glucose decreased	11	0
Alkaline phosphatase increased	11	0.3
Hematology		
Hemoglobin decreased	25	0.6
Neutrophils decreased	24	1.5
Lymphocytes decreased	19	7

a. Severity as defined by the National Cancer Institute CTCAE Version 5.0.

b. The denominator for each laboratory parameter is based on the number of patients with a baseline and post-treatment laboratory value available, which ranged from 325 to 330 patients.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on MODEYSO

Table 6 describes drug interactions where concomitant use of another drug affects MODEYSO.

Table 6: Effect of Other Drugs on MODEYSO

Strong and Moderate CYP3A4 Inhibitors	
Prevention or Management	<ul style="list-style-type: none">• Avoid concomitant use of strong and moderate CYP3A4 inhibitors with MODEYSO.• If concomitant use cannot be avoided for adults and pediatric patients who weigh at least 52.5 kg, reduce the MODEYSO dose as recommended [see <i>Dosage and Administration</i> (2.5)].
Mechanism and Clinical Effects	<ul style="list-style-type: none">• Dordaviprone is a CYP3A4 substrate.• Strong and moderate CYP3A4 inhibitors increase dordaviprone exposure [see <i>Clinical Pharmacology</i> (12.3)], which may increase the risk of MODEYSO-related adverse reactions [see <i>Warnings and Precautions</i> (5.2)].
Strong or Moderate CYP3A4 Inducers	
Prevention or Management	<ul style="list-style-type: none">• Avoid concomitant use of strong and moderate CYP3A4 inducers with MODEYSO.
Mechanism and Clinical Effects	<ul style="list-style-type: none">• Dordaviprone is a CYP3A4 substrate.• Strong and moderate CYP3A4 inducers decrease dordaviprone exposure [see <i>Clinical Pharmacology</i> (12.3)], which may reduce the anti-tumor activity of MODEYSO.

7.2 Drugs Known to Prolong QTc Interval

Table 7 describes drug interactions associated with QTc interval prolongation when used concomitantly with MODEYSO.

Table 7: Products that Prolong QTc Interval

Products that Prolong QTc Interval	
Prevention or Management	<ul style="list-style-type: none">• Avoid concomitant use of MODEYSO with products known to prolong the QTc interval.• If concomitant use cannot be avoided, separate administration of MODEYSO and the QT-prolonging product [see <i>Warnings and Precautions</i> (5.2) and <i>Clinical Pharmacology</i> (12.2)].
	<ul style="list-style-type: none">• MODEYSO causes concentration dependent QTc interval

Clinical Impact	<p>prolongation [see <i>Clinical Pharmacology</i> (12.2)].</p> <ul style="list-style-type: none"> Concomitant use of MODEYSO with other QT-prolonging products may increase the risk of QTc-associated arrhythmias [see <i>Warnings and Precautions</i> (5.2)].
-----------------	--

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from animal studies and its mechanism of action [see *Clinical Pharmacology* (12.1)], MODEYSO can cause fetal harm when administered to a pregnant woman. There are no available data on MODEYSO use in pregnant women to inform a drug-associated risk.

In animal embryo-fetal development studies, oral administration of dordaviprone to pregnant rats and rabbits during the period of organogenesis caused embryofetal mortality, alterations to growth, and structural abnormalities at exposures below the human exposure at the highest recommended dose (see *Data*). Advise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In an embryo-fetal development study, dordaviprone was administered orally to pregnant rats during the period of organogenesis from gestation day 7 to 17 at doses of 25, 62.5, and 125 mg/kg/day. Dordaviprone caused maternal mortality, pre-implantation loss, and embryo-fetal toxicity of absent eye and small renal papillae at the 125 mg/kg/day dose (≥ 2 times the human recommended doses based on body surface area). In an embryo-fetal development study, dordaviprone was administered orally to pregnant rabbits during the period of organogenesis from gestation days 7 to 19 at doses of 10, 25, 62.5, and 100 mg/kg/day. Dordaviprone caused maternal mortality, embryo-fetal mortality, lower fetal weights, and structural malformations of the face, limbs, vessels, brain, and heart at doses of ≥ 10 mg/kg/day (≥ 0.4 times the human exposure at the highest recommended dose based on C_{\max}).

8.2 Lactation

Risk Summary

There are no data on the presence of dordaviprone or its metabolites in human milk, their effects on a breastfed child, or on milk production. Because of the potential for serious adverse reactions in breastfed children from MODEYSO, advise women not to breastfeed during treatment with MODEYSO and for 1 week after the last dose.

8.3 Females and Males of Reproductive Potential

MODEYSO can cause fetal harm when administered to a pregnant woman [see *Use in Specific Populations (8.1)*].

Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to initiating MODEYSO [see *Use in Specific Populations (8.1)*].

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with MODEYSO and for 1 month after the last dose [see *Use in Specific Populations (8.1)*].

Males

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.

Infertility

Based on the mechanism of action of dordaviprone (dopamine D2 receptor inhibition and alterations to mitochondrial function), treatment with MODEYSO may adversely impact fertility in males and females.

8.4 Pediatric Use

The safety and effectiveness of MODEYSO has been established in pediatric patients aged 1 year and older for the treatment of diffuse midline glioma harboring an H3 K27M mutation [see *Adverse Reactions (6.1)* and *Clinical Studies (14)*].

The efficacy of MODEYSO was evaluated in 4 pediatric patients aged 9 to 17 years with diffuse midline glioma harboring an H3 K27M mutation. Safety was evaluated in 154 pediatric patients with glioma aged 3 to 17 years who received MODEYSO at the recommended dose across four open-label clinical studies (ONC006, ONC013, ONC014, and ONC018). Of these 154 patients, 73% were 3 to 11 years of age and 27% were 12 to 17 years of age. No additional safety signals were observed in pediatric patients [see *Adverse Reactions (6.1)*].

The exposure of dordaviprone in pediatric patients weighing 10 kg and higher is predicted to be within the range of exposures predicted in adults at the recommended dosage [see *Clinical Pharmacology (12.3)*].

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

8.5 Geriatric Use

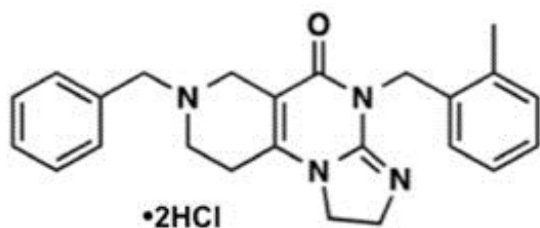
Of the 376 patients with glioma who received MODEYSO at the recommended dose across four open-label clinical studies (ONC006, ONC013, ONC014, and ONC018), 3.7% of patients were ≥ 65 years of age and 0.5% were ≥ 75 years of age. Clinical studies of MODEYSO did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

11 DESCRIPTION

Dordaviprone is a protease activator.

Dordaviprone is present as dordaviprone hydrochloride with the molecular formula $C_{24}H_{26}N_4O \cdot 2HCl$. The molecular weight is 459.41. The full chemical name for dordaviprone hydrochloride is 7-benzyl-4-(2-methylbenzyl)-1,2,6,7,8,9-hexahydroimidazo[1,2-a]pyrido[3,4-e]pyrimidin-5(4*H*)-one dihydrochloride.

Dordaviprone hydrochloride has the following chemical structure:



Dordaviprone hydrochloride is a white to off-white solid that is freely soluble in water. The 1% solution of dordaviprone hydrochloride is measured as pH 3.3.

MODEYSO (dordaviprone) capsules are supplied as 125 mg strength capsules in an immediate-release oral formulation. Each MODEYSO capsule contains 125 mg of dordaviprone (equivalent to 148.8 mg of dordaviprone hydrochloride).

The inactive ingredients in the capsule include magnesium stearate, microcrystalline cellulose, and sodium starch glycolate. The capsule shell consists of hypromellose and titanium dioxide. The black printing ink contains alcohol, D&C yellow #10, FD&C blue #1, FD&C blue #2, FD&C red #40, ferrousferic oxide, methyl alcohol, *N*-butyl alcohol, propylene glycol, and shellac glaze (20% esterified).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Dordaviprone is a protease activator of the mitochondrial caseinolytic protease P (ClpP). Dordaviprone 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, dordaviprone 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.

Dordaviprone exhibited antitumor activity in cell-based assays and in vivo models of H3 K27M-mutant diffuse glioma.

12.2 Pharmacodynamics

Cardiac Electrophysiology

At 1.2 times the maximum recommended dose, the estimated mean QTcF change was

11.8 msec (90% CI: 9.8, 13.7) [see *Warnings and Precautions (5.2)* and *Drug Interactions (7.2)*].

Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of dordaviprone have not been fully characterized.

12.3 Pharmacokinetics

Dordaviprone pharmacokinetics were predicted following a single dose in patients at the approved recommended dosage and are presented as mean (CV%) unless otherwise specified. Dordaviprone maximum concentration (C_{max}) is 2.8 mcg/mL (42%), and total systemic exposure (AUC) is 23 hr·mcg/mL (48%). Dordaviprone C_{max} and AUC increased in a dose proportional manner over the dose range of 125 to 625 mg. No accumulation is observed following once weekly dosing.

Absorption

Dordaviprone median (min, max) time to maximum plasma concentration (T_{max}) is 1.4 hours (0.5, 5.6 hours).

Food Effect

Dordaviprone C_{max} decreased by 40% with no change on AUC following administration with a high-fat meal (800 to 1,000 calories, 50% fat).

Distribution

Dordaviprone apparent (oral) volume of distribution is 450 L (40%).

Dordaviprone plasma protein binding is 95% to 97% and independent of concentrations in vitro.

The median blood-to-plasma ratio is 0.67 in vitro.

Metabolism

Dordaviprone is primarily metabolized by CYP3A4 with minor contribution from CYP2B6, CYP2C8, CYP2C9, CYP2D6, and CYP3A5.

Excretion

Dordaviprone mean terminal half-life is 11 hours (30%), and the apparent clearance is approximately 27 L/hr (48%).

Following a single dose of radiolabeled dordaviprone, 70% of the dose was recovered in urine and 20% in feces with no notable unchanged dordaviprone in urine or feces.

Specific Populations

No clinically significant differences in the pharmacokinetics of dordaviprone were observed based on age (3 to 90 years), sex, race (74% White, 9% Black or African American, or 5% Asian) or mild hepatic impairment (total bilirubin \leq ULN with AST $>$ ULN or total bilirubin >1 to 1.5 times ULN with any AST).

The effect of severe hepatic impairment (total bilirubin >3 times ULN with any AST) on dordaviprone pharmacokinetics is unknown.

Pediatric Patients

The exposure of dordaviprone in pediatrics weighing 10 kg and higher is predicted to be within the range of exposures predicted in adults at the recommended dosage.

Renal Impairment

Following a single oral dose of 375 mg (0.6 times the maximum approved recommended dose), dordaviprone AUC increased by 1.5-fold and C_{max} by 1.1-fold in subjects with severe renal impairment ($CL_{cr} < 30$ mL/min, estimated by the Cockcroft-Gault equation).

Hepatic Impairment

Following a single oral dose of 125 mg (0.2 times the maximum approved recommended dose) dordaviprone AUC increased by 1.5-fold and C_{max} by 1.2-fold in subjects with moderate hepatic impairment (Child Pugh class B).

Drug Interaction Studies

Clinical Studies and Model-Informed Approaches

CYP3A4 Inhibitors: Dordaviprone C_{max} increased by 2-fold and AUC increased by 4-fold following concomitant administration of itraconazole (strong CYP3A4 inhibitor) 200 mg once daily for 8 days.

Dordaviprone C_{max} is predicted to increase by ~1.5-fold and AUC by 2.5-fold following concomitant administration of fluconazole or erythromycin (moderate CYP3A4 inhibitor).

CYP3A4 Inducers: Dordaviprone C_{max} is predicted to decrease by 68% and AUC by 83% following concomitant administration of rifampin (strong CYP3A4 inducer) and dordaviprone C_{max} is predicted to decrease by 44% and AUC by 65% following concomitant administration of efavirenz (moderate CYP3A4 inducer).

Other Drugs: No clinically significant difference in dordaviprone pharmacokinetics is predicted when used concomitantly with cimetidine (weak CYP3A4 inhibitor).

No clinically significant difference in dordaviprone pharmacokinetics is observed with multiple doses of a rabeprazole (proton-pump inhibitor).

No clinically significant differences in the pharmacokinetics of the following drugs are predicted following concomitant use with MODEYSO: dabigatran etexelate (P-gp substrate), rosuvastatin (BCRP substrate), midazolam (CYP3A substrate), desipramine (CYP2D6 substrate) and repaglinide (CYP2C8 substrate).

In Vitro Studies

CYP Enzymes: Dordaviprone inhibits CYP1A2, CYP2B6, and CYP2C19 and induces CYP2B6.

Transporter Systems: Dordaviprone inhibits MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OATP1B3, and OCT1.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity studies with dordaviprone were not conducted.

Mutagenesis

Dordaviprone was not genotoxic in in vitro (Ames and micronucleus assay) and in vivo (mouse micronucleus) assays.

Impairment of Fertility

Dedicated fertility studies were not conducted with dordaviprone.

13.2 Animal Toxicology and/or Pharmacology

The nonclinical safety profile of dordaviprone reflects the on-target pharmacology and dopamine receptor inhibition. In repeat-dose toxicology studies of up to 13 weeks in duration, weekly oral administration of dordaviprone to dogs caused central nervous system-related toxicities including whole body tremors, cranial tremors, seizures, excessive salivation, lateral recumbency, rigidity, paddling of limbs, overall rigid body, salivation, abnormal gait/stance, and twitching at doses resulting in less than or equal to 0.7 times the human exposure at the highest recommended dose based on AUC. In a 13-week repeat-dose toxicology study in rats, mammary gland hyperplasia occurred at doses resulting in 0.11 times the human exposure at the highest recommended dose based on AUC.

14 CLINICAL STUDIES

The efficacy of MODEYSO was evaluated in adult and pediatric patients with glioma across five open-label, non-randomized clinical studies conducted in the U.S. (ONC006 [NCT02525692], ONC013 [NCT03295396], ONC014 [NCT03416530], ONC016 [NCT05392374], and ONC018 [NCT03134131]). Pre-specified criteria were defined to establish an integrated efficacy population; eligible patients were required to have received single-agent MODEYSO, have diffuse midline glioma harboring an H3 K27M mutation with progressive and measurable disease per Response Assessment in Neuro-Oncology-High Grade Glioma (RANO-HGG) criteria, be ≥ 90 days post-radiation therapy, have adequate washout from prior anticancer therapies, have a Karnofsky Performance Status/Lansky Performance Status (KPS/LPS) score ≥ 60 , and have stable or decreasing corticosteroid use. Patients with diffuse intrinsic pontine glioma (DIPG), primary spinal tumors, atypical histologies, or cerebrospinal fluid dissemination were excluded. Patients received weight-based dosing of MODEYSO until disease progression or unacceptable toxicity.

The integrated efficacy population included 50 patients who met these criteria. The major efficacy outcome measure was overall response rate (ORR) assessed by blinded independent central review (BICR) according to RANO 2.0 criteria. Additional efficacy outcome measures were BICR-assessed ORR according to RANO-HGG criteria and Response Assessment in Neuro-Oncology-Low Grade Glioma (RANO-LGG) criteria, duration of response, and time to response.

Baseline demographics were: median age 31 years (range: 9 to 70) with 6% younger than 17 years of age; 46% female; 80% White, 6% Black or African American, 2% Asian, 10% other races, and 2% race unknown; 8% were of Hispanic or Latino ethnicity; 72% had KPS/LPS 80 to 100. Relevant disease characteristics included 72% treated at first recurrence, 28% had 2 or more recurrences; primary tumor location was thalamic in 52% and non-thalamic midline region in 48%; 88% received prior temozolomide; 62%

were receiving corticosteroids at baseline; median time from end of prior radiation was 7.4 months (range: 3.0 to 102.1).

Efficacy results are shown in Table 8.

Table 8: Efficacy Results for Patients with Diffuse Midline Glioma Harboring an H3 K27M Mutation in Studies ONC006, ONC013, ONC014, ONC016, and ONC018 per RANO 2.0

Efficacy Parameter	MODEYSO N=50
Overall Response Rate (95% CI)^a	22% (12, 36)
Partial response (PR)	16%
Minor response (MR)	6%
Duration of Response	N=11
Median (95% CI) ^b , months	10.3 (7.3, 15.2)
% with observed DOR ≥6 months ^c	73%
% with observed DOR ≥12 months ^c	27%

Abbreviations: BICR=blinded independent central review; CI=confidence interval; RANO=Response Assessment in Neuro-Oncology.

a. Confirmed overall response rate assessed by BICR; CI based on Clopper-Pearson method.

b. Based on Kaplan-Meier estimate.

c. Based on observed time.

Among responders, the median time to response was 3.6 months (range 1.6, 15.6).

Using BICR-assessed RANO 2.0 criteria, there was one additional responder based on the integrated response assessment, which takes into account corticosteroid use and performance status. Based on BICR-assessed RANO-HGG criteria (n=50), the ORR was 20% (95% CI: 10, 34), with 1 complete and 9 partial responses. Based on BICR-assessed RANO-LGG criteria (n=50), the ORR was 20% (95% CI: 10, 34), with 5 partial and 5 minor responses.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Strength	Description	Package Configuration	NDC Number
125 mg	White, opaque, hard capsules printed with “DDP” and “125” on the body and “CMRX” on the cap of the capsule.	Each bottle contains 10 capsules and desiccant with a child-resistant closure.	68727-250-01

Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient and caregiver to read the FDA-approved patient labeling (*Patient Information and Instructions for Use*).

Hypersensitivity

Advise patients that MODEYSO can cause hypersensitivity. Inform patients about the signs and symptoms of hypersensitivity reactions and instruct patients or caregivers to seek immediate medical attention if symptoms occur [see *Warnings and Precautions (5.1)*].

QTc Interval Prolongation

Advise patients that MODEYSO can cause QTc interval prolongation. Inform patients of the signs and symptoms of QTc prolongation and instruct patients or caregivers to seek immediate medical attention if symptoms occur [see *Warnings and Precautions (5.2)*].

Drug Interactions

Inform patients that MODEYSO may interact with some drugs. Advise patients to inform their healthcare provider about all medications they are taking, including prescription and over-the-counter drugs, vitamins, and herbal products. Additionally, patients should consult their healthcare provider before starting or stopping any prescription drug, nonprescription drug, or supplement [see *Drug Interactions (7)*].

Administration

Instruct patients and caregivers to read the *Instructions for Use* before taking MODEYSO, and each time the patient gets a refill as there may be new information they need to know.

Patients should take MODEYSO orally once weekly on an empty stomach (no food intake at least 1 hour prior to or 3 hours after taking MODEYSO). Take the prescribed dose at the same time on the same day of the week [see *Dosage and Administration (2.3)* and *Clinical Pharmacology (12.3)*].

Instruct patients to swallow capsules whole. For patients unable to swallow capsules whole, instruct patients to open capsules and mix contents with approximately 15 to 30 mL of liquid (sports drink, apple juice, lemonade, or water). Instruct patients to drink the mixture. After drinking the mixture, instruct patients to add another 15 to 30 mL of the liquid to the container, swirl to dissolve any remaining medication, and then drink the remaining contents [see *Dosage and Administration (2.3)* and *Instructions for Use*].

Embryo-fetal Toxicity

Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

Advise females to inform their healthcare provider of a known or suspected pregnancy [see *Warnings and Precautions (5.3)* and *Use in Specific Populations (8.1, 8.3)*].

Advise females of reproductive potential to use effective contraception during treatment

with MODEYSO and for 1 month after the last dose [see *Use in Specific Populations* (8.3)].

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 [see *Use in Specific Populations* (8.3)].

Lactation

Advise women not to breastfeed during treatment with MODEYSO and for 1 week after the last dose [see *Use in Specific Populations* (8.2)].

Distributed by:

Jazz Pharmaceuticals, Inc.

Palo Alto, CA 94306

Patient Package Insert

<p>PATIENT INFORMATION MODEYSO (moh-DAY-soh) (dordaviprone) capsules, for oral use</p>
--

What is MODEYSO?

MODEYSO is a prescription medicine used to treat adults and children 1 year of age and older with a certain type of brain tumor called diffuse midline glioma that has a specific “H3 K27M” gene mutation **and** has worsened after other treatments.

It is not known if MODEYSO is safe and effective in children less than 1 year of age.

Before taking MODEYSO, tell your healthcare provider about all your medical conditions, including if you:

- have heart failure or heart rhythm problems, including QT prolongation and long QT syndrome.
- are pregnant or plan to become pregnant. MODEYSO can harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with MODEYSO.
 - o Your healthcare provider should check to see if you are pregnant before you begin treatment with MODEYSO.
 - o **Females who are able to become pregnant** should use effective birth control (contraception) during treatment with MODEYSO and for 1 month after your last dose.
 - o **Males with partners who are able to become pregnant** should use effective contraception during treatment with MODEYSO and for 1 month after your last dose.
- are breastfeeding or plan to breastfeed. It is not known if MODEYSO passes into breast milk. Do not breastfeed during treatment with MODEYSO and for 1 week after your last dose. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. MODEYSO and other medicines may affect the way each other work and may cause serious side effects. You can ask your healthcare provider or pharmacist for a list of medications that interact with MODEYSO.

Know the medicines you take. Keep a list of your medicines to show your healthcare provider and pharmacist. **Do not** start or stop taking any new medicines without first talking to your healthcare provider.

How should I take MODEYSO?

- Take MODEYSO exactly as your healthcare provider tells you.
- Do not change your dose or stop taking MODEYSO without talking to your healthcare provider.
- Your healthcare provider may change your dose, temporarily stop, or completely stop treatment with MODEYSO if you develop certain side effects.
- Take MODEYSO 1 time each week on the same day of the week. Take all of the capsules prescribed for your dose at the same time.
- Take MODEYSO on an empty stomach, at least 1 hour before or 3 hours after eating food.
- Swallow MODEYSO capsules whole. If the capsules cannot be swallowed whole, see the detailed **Instructions for Use** for how to prepare and take or give MODEYSO as a liquid.
- If vomiting happens after taking a dose of MODEYSO, do not take another dose. Take the next dose of MODEYSO on the next regularly scheduled weekly day of the week.
- If you miss a weekly dose of MODEYSO by:
 - **2 days or less**, take the missed dose as soon as you remember. Take the next dose of MODEYSO on the next regularly scheduled day of the week.
 - **More than 2 days**, skip the missed dose and take the next dose of MODEYSO on the next regularly scheduled day of the week.

What are the possible side effects of MODEYSO?

MODEYSO may cause serious side effects, including:

- **Allergic reactions.** Allergic reactions may happen during treatment with MODEYSO and can be severe. Stop taking MODEYSO and get immediate emergency medical help right away if you get any signs or symptoms of allergic reactions, including:
 - rash
 - hives
 - fever
 - feeling faint or dizzy
 - wheezing or trouble breathing
 - swelling of the face or throat
- **Heart rhythm problems (QTc interval prolongation).** MODEYSO can cause changes in the electrical activity of your heart and can increase your chance of getting a type of abnormal heart rhythm that can lead to sudden death called torsades de pointes. Before you start treatment and during treatment as needed,

your healthcare provider will check your heart using an electrocardiograph (ECG) and check your blood levels of salts called electrolytes. Get emergency medical help right away if you get any signs or symptoms of abnormal heart rhythm, including:

- o feeling lightheaded or faint
- o dizziness
- o fast heartbeat
- o heart palpitations
- o shortness of breath

The most common side effects of MODEYSO include:

- tiredness
- headache
- vomiting
- nausea
- muscle, joint, and bone pain

The most common abnormal blood tests include decreased white blood cells, decreased red blood cells, decreased calcium, and increased liver enzymes. MODEYSO may cause fertility problems in males and females, which may affect your ability to have children. Talk to your healthcare provider if this is a concern for you. These are not all of the possible side effects of MODEYSO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Chimerix, Inc. at 1-866-662-2679.

How should I store MODEYSO?

- Store MODEYSO at room temperature between 68°F to 77°F (20°C to 25°C).
- The MODEYSO bottle has a child-resistant closure.

Keep MODEYSO and all medicines out of the reach of children.

General information about the safe and effective use of MODEYSO.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use MODEYSO for a condition for which it was not prescribed. Do not give MODEYSO to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about MODEYSO that is written for health professionals.

What are the ingredients in MODEYSO?

Active ingredient: dordaviprone

Inactive ingredients: magnesium stearate, microcrystalline cellulose, and sodium starch glycolate. The capsule shell contains hypromellose and titanium dioxide. The black printing ink contains alcohol, D&C yellow #10, FD&C blue #1, FD&C blue #2, FD&C red #40, ferrousferrous oxide, methyl alcohol, N-butyl alcohol, propylene glycol, and shellac glaze (20% esterified).

Distributed by:

Jazz Pharmaceuticals, Inc.

Palo Alto, CA 94306

For more information, contact Chimerix, Inc. at 1-866-662-2679.

Instructions for Use

INSTRUCTIONS FOR USE MODEYSO [moh-DAY-soh] (dordaviprone) capsules, for oral use

This Instructions for Use contains information on how to prepare and take or give MODEYSO capsules as a liquid.

Read this Instructions for Use carefully before you prepare and take or give a dose of MODEYSO for the first time and each time you or your child gets a prescription refill. There may be new information. This information does not take the place of talking with your healthcare provider about your or your child's medical condition or treatment.

Important Information You Need to Know Before Preparing and Taking or Giving MODEYSO Capsules as a Liquid.

- For oral use only (take by mouth).
- Take or give MODEYSO exactly as your healthcare provider tells you. Do not change the dose or stop taking MODEYSO without talking to your healthcare provider.
- Take or give MODEYSO 1 time each week on the same day of the week. Take or give all of the capsules prescribed for your dose at the same time.
- Take or give MODEYSO on an empty stomach, at least 1 hour before or 3 hours after eating food.
- If you or your child cannot swallow the capsules whole, the capsules can be dissolved in sports drink, apple juice, lemonade, or water and taken as a liquid.
- Check the expiration date on the MODEYSO bottle. Do not take or give MODEYSO if the expiration date has passed. Contact your pharmacist if the medicine is expired.
- Do not take or give MODEYSO if the bottle or the capsules are broken or damaged. Contact your healthcare provider or pharmacist for a replacement.

Supplies needed to prepare and dissolve MODEYSO capsules to take or give as a liquid.

Bottle of
MODEYSO
capsules



1 TABLESPOON
(TBSP)



LIQUID
Sports Drink, Apple Juice,
Lemonade, or Water



SMALL CUP

Section A: Preparing and dissolving MODEYSO capsules to take or give as a liquid

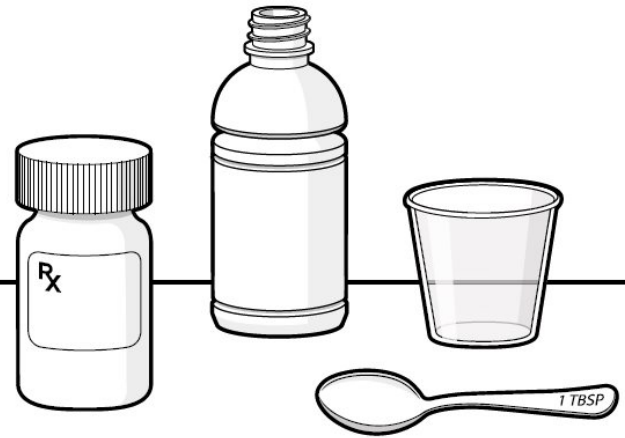
Preparing to dissolve the capsules

Step 1:

Wash and dry your hands.

Place the MODEYSO bottle on a clean, flat surface.

Gather the rest of the supplies you will need so they are ready to use.



Step 2:

Check the prescribed dose. Count out the number of MODEYSO capsules needed for the dose.



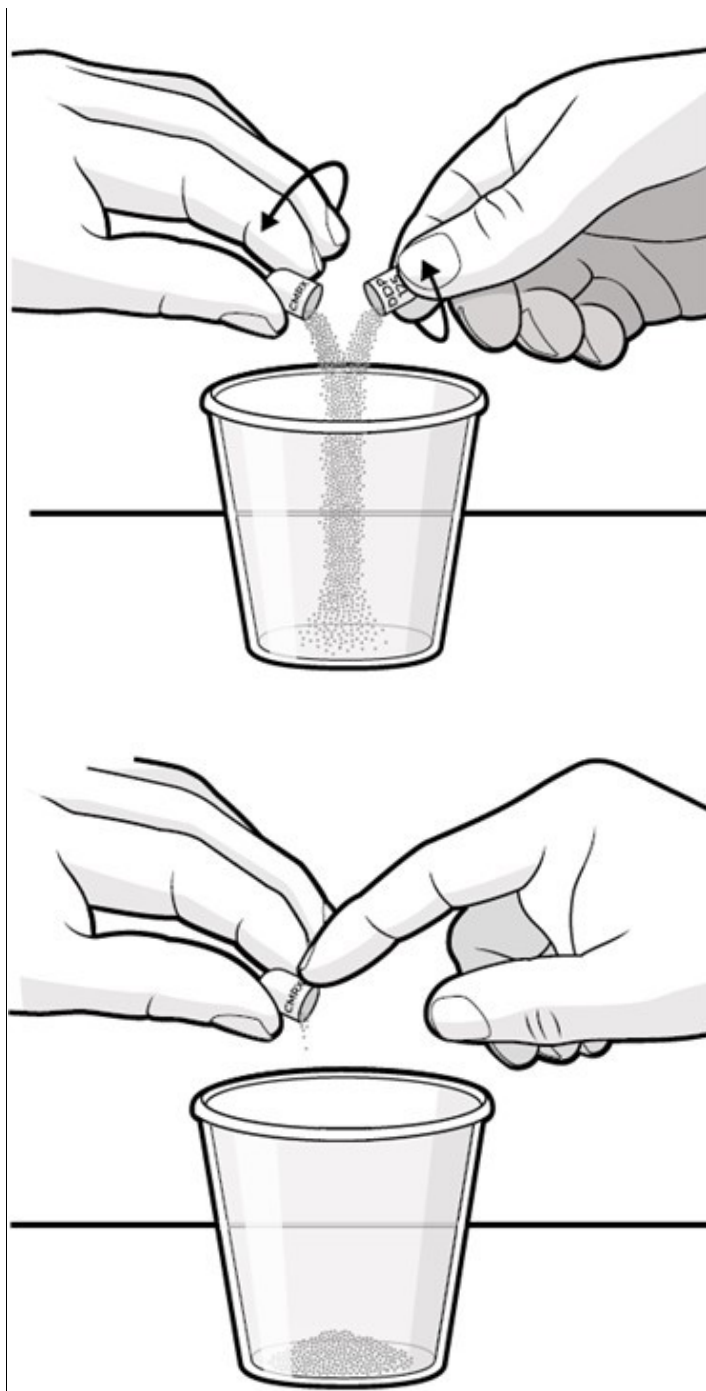
Opening the capsules

Step 3:

Hold the capsule over a clean, empty cup. Carefully open the capsule by gently pulling and twisting both ends.

Slowly empty the contents (powder) into the cup.

If any powder remains inside the capsule shell, gently tap the shell over the cup to remove any remaining powder.



Step 4:

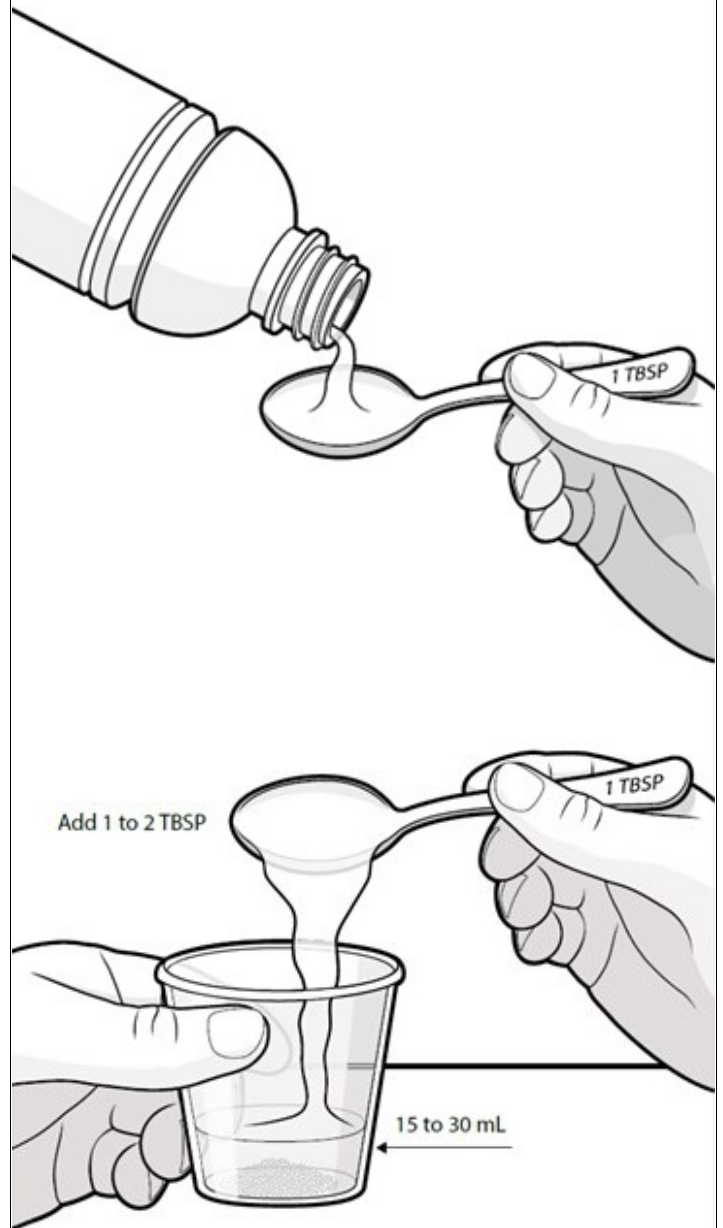
Repeat **Step 3** for each additional capsule needed for the prescribed dose.

Dissolving the capsules in liquid

Step 5:

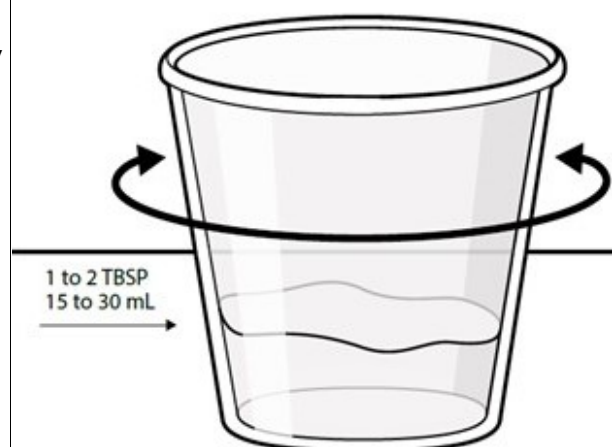
Use a tablespoon (15 mL) to measure the liquid.

Add **1 to 2** tablespoons (about 15 mL to 30 mL) of your chosen liquid (sports drink, apple juice, lemonade, or water) to the cup.



Step 6:

Gently swirl the liquid around the cup before taking or giving the mixture until no large chunks of powder remain. The mixture may look cloudy. This is normal and okay.



Section B: Taking or giving a dose of MODEYSO as a liquid

Step 7:

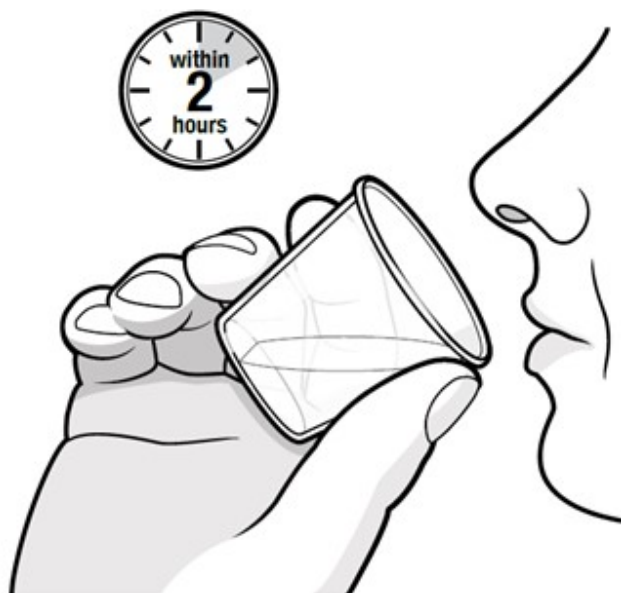
Take or give all of the mixture as soon as possible. Always take or give the mixture within 2 hours of preparing it.

An oral dosing syringe may be used to take or give the mixture by mouth. Refer to Section D for detailed instructions.

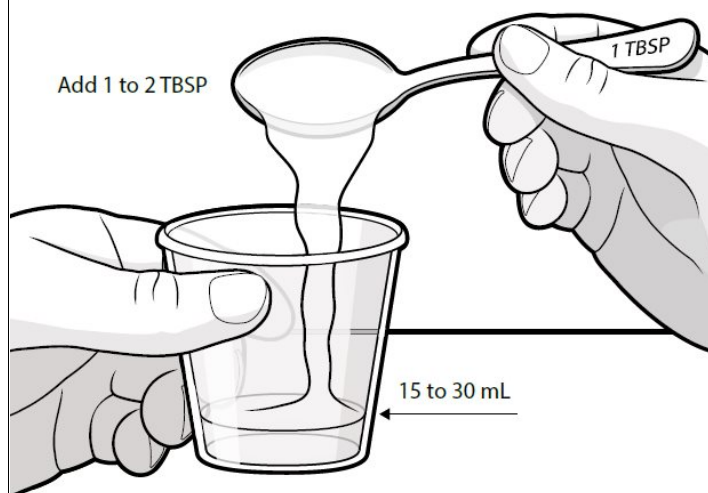
The mixture may be taken or given through a feeding tube. Refer to Section E for detailed instructions.

Throw away the mixture if it is not taken within 2 hours of preparing it and go back to Section A to prepare a new dose.

If vomiting happens after taking or giving the dose, or not all of the liquid is swallowed, **do not** take or give another dose. Take the next dose of MODEYSO on the next regularly scheduled day of the week.

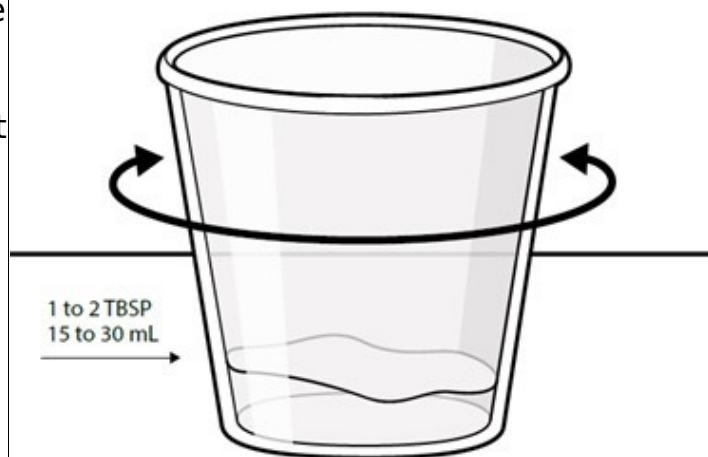
**Step 8:**

After taking or giving the dose, add **1 to 2** more tablespoons (about 15 mL to 30 mL) of your chosen liquid to the cup.

**Step 9:**

Swirl the liquid around the cup to make sure any remaining medicine is mixed with the liquid.

This helps make sure that no medicine is left behind.

**Step 10:**

Repeat **Step 7**.

Section C: Disposing of (throwing away) empty MODEYSO capsule shells and cleaning the cup

Step 11:

After taking or giving the dose, throw empty capsule shells in the trash.
Do not save or reuse empty capsules.



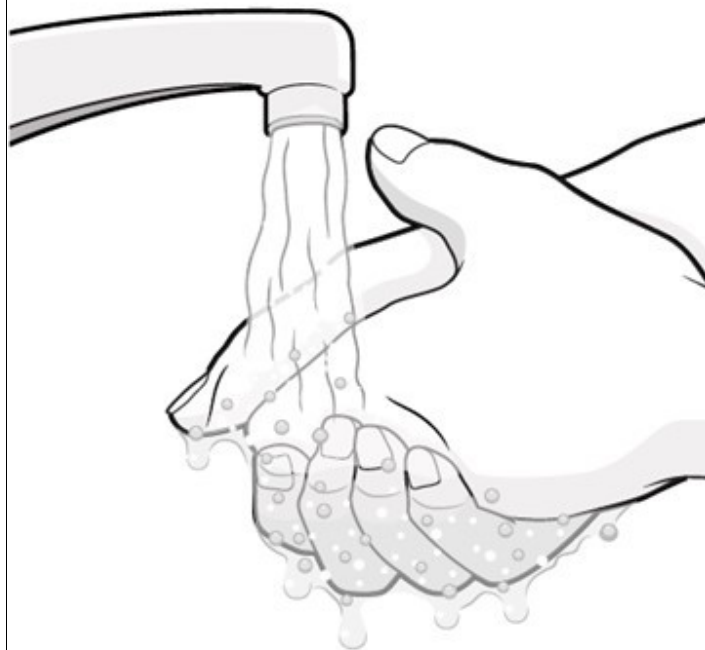
Step 12:

After taking or giving the dose, rinse the cup with warm running water to remove all remaining medicine.



Step 13:

Wash your hands with soap and water.

**Section D: Taking or giving a dose of MODEYSO as a liquid using an oral dosing syringe**

If you are using an oral dosing syringe to take or give MODEYSO by mouth:

1. Follow **Steps 1 through 6 in Section A** to prepare the MODEYSO liquid mixture in a cup.
2. If there is a cap, remove the cap of the oral dosing syringe.
3. Push the plunger down into the oral dosing syringe as far as it will go.
4. Place the oral dosing syringe tip in the mixture in the cup. Pull up on the plunger to draw all the mixture into the oral dosing syringe.
5. You or your child should sit upright to take or give a dose of MODEYSO. Place the tip of the oral dosing syringe towards the inside of the cheek in your or your child's mouth.
6. Slowly push the medicine into the mouth by pressing down on the plunger, allowing time for swallowing. Do not forcefully push the plunger. This may cause choking.
7. You or your child may drink other liquids right away after swallowing the mixture.
8. **Steps 3 through 7 in this section** may be repeated until all the mixture has been taken or given.
9. After taking or giving the dose, add 1 to 2 more tablespoons (about 15 mL to 30 mL) of your chosen liquid to the cup.
10. Swirl the liquid around the cup to make sure any remaining medicine is mixed with the liquid. This helps make sure that no medicine is left behind.
11. Using the oral dosing syringe, repeat **Steps 3 through 6 in this section** until all of the mixture in the cup has been taken or given.
12. After completing **Step 11 in this section**, remove the plunger from the oral dosing syringe and rinse each part with warm running water to remove all remaining medicine. Allow the parts to air dry completely before putting the syringe back together.

Refer to **Section C: Disposing of (throwing away) empty MODEYSO capsule shells and cleaning the cup.**

Section E: Taking or giving a dose of MODEYSO as a liquid using a feeding

tube

MODEYSO may be given through a naso-gastric (“ng”) or gastrostomy (“g”) feeding tube, as directed by your healthcare provider.

1. Follow **Steps 1 through 6 in Section A** to prepare the MODEYSO liquid mixture in a cup.
2. Flush the feeding tube according to the manufacturer's instructions before each dose.
3. Draw up the mixture into a catheter tip syringe.
4. Connect the syringe containing the mixture to the feeding tube.
5. Apply slow, steady pressure to the plunger to give all the contents of the syringe through the feeding tube.
6. After giving the dose, add 1 to 2 more tablespoons (about 15 mL to 30 mL) of your chosen liquid to the cup.
7. Swirl the liquid around the cup to make sure any remaining medicine is mixed with the liquid. This helps make sure that no medicine is left behind.
8. Using the syringe, repeat **Steps 3 through 5 in this section** until all the mixture in the cup has been given.
9. After completing **Step 8 in this section**, flush the feeding tube according to the manufacturer's instructions.
10. After completing **Step 9 in this section**, remove the plunger from the syringe and rinse each part with warm running water to remove all remaining medicine. Allow the parts to air dry completely before putting the syringe back together.

Refer to **Section C: Disposing of (throwing away) empty MODEYSO capsule shells and cleaning the cup.**

Storing MODEYSO

- Store MODEYSO at room temperature between 68°F to 77°F (20°C to 25°C).
- The MODEYSO bottle has a child-resistant closure.

Keep MODEYSO and all medicines out of the reach of children.

Distributed by:

Jazz Pharmaceuticals, Inc.
Palo Alto, CA 94306

For more information, contact Chimerix, Inc. at 1-866-662-2679.

This Instructions for Use has been approved by the U.S. Food and Drug Administration. Issued: 08/2025

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

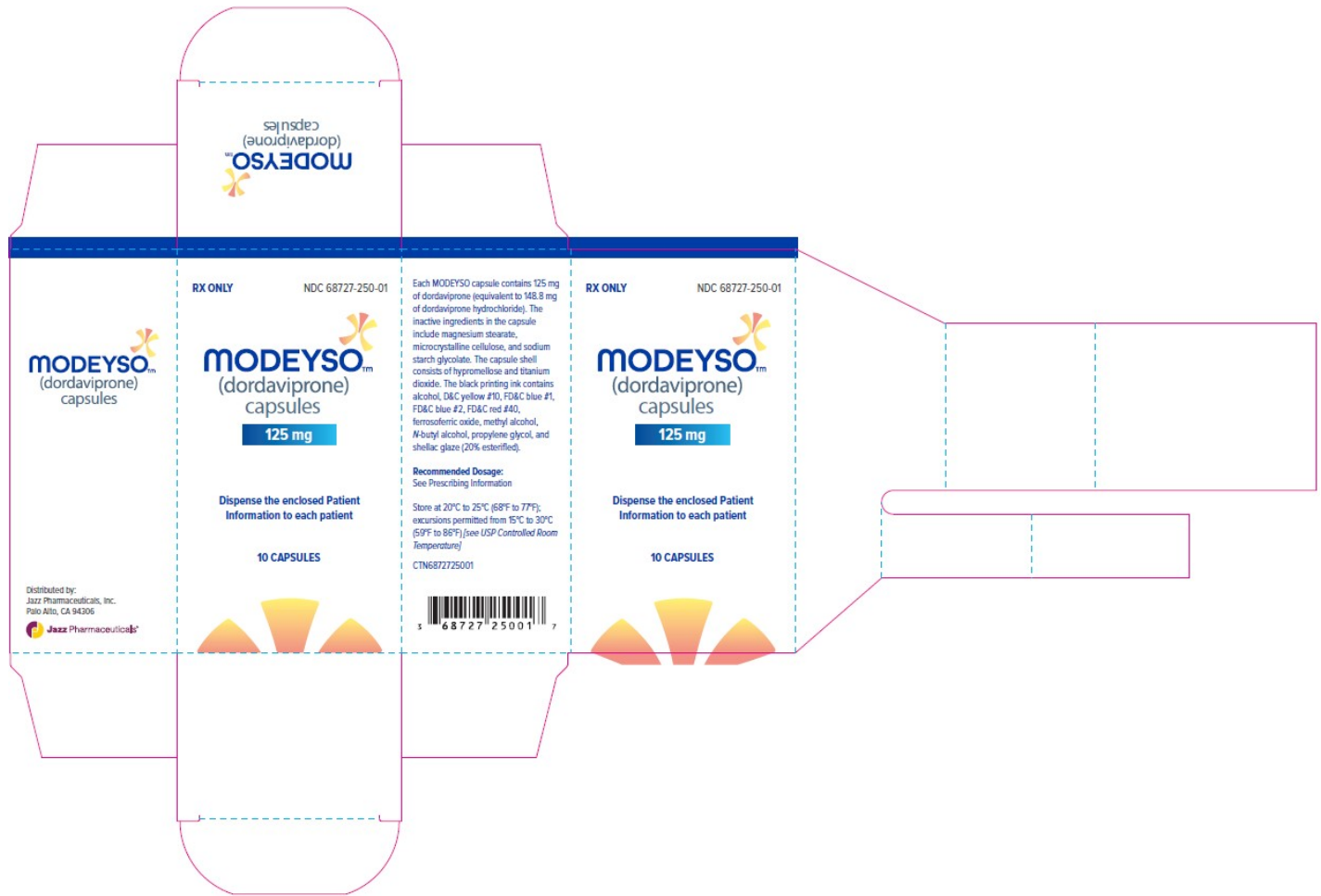
RX ONLY

MODEYSO™
(dordaviprone)

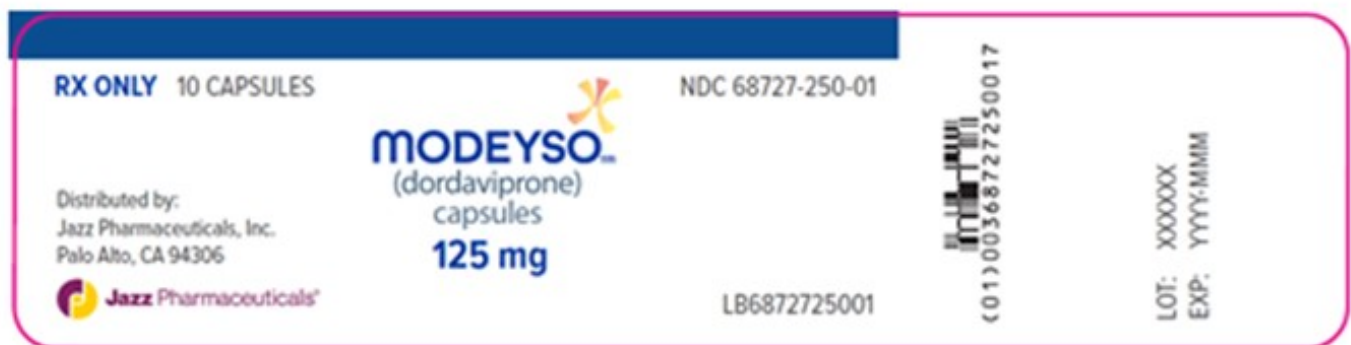
125 mg
10 CAPSULES

FOR ORAL USE

See Full Prescribing Information
For MODEYSO Inside



PACKAGE/LABEL PRINCIPAL DISPLAY PANEL



MODEYSO
dordaviprone capsule

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:68727-250
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
DORDAVIPRONE (UNII: 9U35A31JAI) (DORDAVIPRONE - UNII:9U35A31JAI)	DORDAVIPRONE	125 mg

Inactive Ingredients	
Ingredient Name	Strength
MICROCRYSTALLINE CELLULOSE 112 (UNII: X7XJ6RM9Q2)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	

Product Characteristics			
Color	WHITE	Score	no score
Shape	CAPSULE	Size	16mm
Flavor		Imprint Code	CMRX;DDP;125
Contains			

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:68727-250-01	1 in 1 CARTON	08/06/2025	
1		10 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA219876	08/06/2025	

Labeler - Jazz Pharmaceuticals, Inc. (135926363)

Establishment			
Name	Address	ID/FEI	Business Operations
API, Inc.		048504349	API MANUFACTURE(68727-250)

Establishment

Name	Address	ID/FEI	Business Operations
Robertson Microlit Laboratories, Inc.		177250289	ANALYSIS(68727-250)

Establishment

Name	Address	ID/FEI	Business Operations
Frontida BioPharm, LLC		080243260	MANUFACTURE(68727-250) , ANALYSIS(68727-250) , PACK(68727-250) , LABEL(68727-250)

Establishment

Name	Address	ID/FEI	Business Operations
Frontage Laboratories, Inc.		832653625	ANALYSIS(68727-250)

Revised: 8/2025

Jazz Pharmaceuticals, Inc.