

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

ODOMZO® (sonidegib) capsules, for oral use

Initial U.S. Approval: 2015

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ODOMZO is a hedgehog pathway inhibitor indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy. (1)
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Recommended dosage: 200 mg orally once daily taken on an empty stomach, at least 1 hour before or 2 hours after a meal. (2.2)
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200 mg capsules (3)
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None. (4)

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<ul style="list-style-type: none">• Embryo-Fetal Toxicity: Advise patients not to donate blood or blood products during treatment with ODOMZO and for at least 20 months after the last dose. (5.1)• Musculoskeletal Adverse Reactions: Obtain serum creatine kinase (CK) and creatinine levels prior to initiating therapy, periodically during treatment, and as clinically indicated. Temporary dose interruption or discontinuation of ODOMZO may be required based on the severity of musculoskeletal adverse reactions. (2.2, 5.2)• Premature fusion of the epiphyses (5.3, 8.4)

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The most common adverse reactions occurring in ≥10% of patients are muscle spasms, alopecia, dysgeusia, fatigue, nausea, musculoskeletal pain, diarrhea, decreased weight, decreased appetite, myalgia, abdominal pain, headache, pain, vomiting, and pruritus. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sun Pharmaceutical Industries, Inc. at 1-800-406-7984 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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<ul style="list-style-type: none">• CYP3A inhibitors: Avoid strong CYP3A inhibitors. Avoid long-term (greater than 14 days) use of moderate CYP3A inhibitors. (7.1)• CYP3A inducers: Avoid strong and moderate CYP3A inducers. (7.1)
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<ul style="list-style-type: none">• Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 08/2022

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FULL PRESCRIBING INFORMATION

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1 INDICATIONS AND USAGE

ODOMZO (sonidegib) is indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Important Safety Information

Verify the pregnancy status of females of reproductive potential prior to initiating ODOMZO [see *Use in Specific Populations* (8.1, 8.3)].

2.2 Recommended Dosage

The recommended dosage of ODOMZO is 200 mg taken orally once daily on an empty stomach, at least 1 hour before or 2 hours after a meal, administered until disease progression or unacceptable toxicity [see *Clinical Pharmacology* (12.3)].

Obtain serum creatine kinase (CK) levels and renal function tests prior to initiating ODOMZO in all patients [see *Dosage and Administration* (2.2) and *Warnings and Precautions* (5.2)]. If a dose of ODOMZO is missed, resume dosing with the next scheduled dose.

2.3 Dosage Modifications for Adverse Reactions

Interrupt ODOMZO for

- Severe or intolerable musculoskeletal adverse reactions.
- First occurrence of serum CK elevation between 2.5 and 10 times upper limit of normal (ULN).
- Recurrent serum CK elevation between 2.5 and 5 times ULN.

Resume ODOMZO at 200 mg daily upon resolution of clinical signs and symptoms.

Permanently discontinue ODOMZO for

- Serum CK elevation greater than 2.5 times ULN with worsening renal function.
- Serum CK elevation greater than 10 times ULN.
- Recurrent serum CK elevation greater than 5 times ULN.
- Recurrent severe or intolerable musculoskeletal adverse reactions.

3 DOSAGE FORMS AND STRENGTHS

Capsules: 200 mg, opaque pink colored with ‘SONIDEGIB 200MG’ printed on the body and ‘NVR’ printed on the cap in black ink (equivalent to 281 mg of diphosphate salt of sonidegib).

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Embryo-Fetal Toxicity

ODOMZO can cause embryo-fetal death or severe birth defects when administered to a pregnant woman. In animal reproduction studies, sonidegib was embryotoxic, fetotoxic, and teratogenic at maternal exposures below the recommended human dose of 200 mg [see *Use in Specific Populations* (8.1)].

Females of Reproductive Potential

Verify pregnancy status of females of reproductive potential prior to initiating ODOMZO treatment. Advise pregnant women of the potential risk to a fetus. Advise females to use effective contraception during treatment with ODOMZO and for at least 20 months after the last dose [see *Use in Specific Populations* (8.3)].

Males

Advise male patients with female partners to use condoms, even after a vasectomy, during treatment with ODOMZO and for at least 8 months after the last dose to avoid potential drug exposure in pregnant females or females of reproductive potential [see *Use in Specific Populations* (8.3)].

Blood Donation

Advise patients not to donate blood or blood products while taking ODOMZO and for at least 20 months after the last dose of ODOMZO, because their blood or blood products might be given to a female of reproductive potential.

5.2 Musculoskeletal Adverse Reactions

Musculoskeletal adverse reactions, which may be accompanied by serum creatine kinase (CK) elevations, occur with ODOMZO and other drugs which inhibit the hedgehog (Hh) pathway.

In a pooled safety analysis of 12 clinical studies involving 571 patients with various advanced cancers treated with ODOMZO at doses ranging from 100 mg to 3000 mg, rhabdomyolysis (defined as serum CK increase of more than ten times the baseline value with a concurrent 1.5-fold or greater increase in serum creatinine above baseline value) occurred in one patient (0.2%) treated with ODOMZO 800 mg.

In the BOLT study, musculoskeletal adverse reactions occurred in 68% (54/79) of patients treated with ODOMZO 200 mg daily with 9% (7/79) reported as Grade 3 or 4. The most frequent manifestations of musculoskeletal adverse reactions reported as an adverse event were muscle spasms (54%), musculoskeletal pain (32%), and myalgia (19%). Increased serum CK laboratory values occurred in 61% (48/79) of patients with 8% (6/79) of patients having Grade 3 or 4 serum CK elevations. Musculoskeletal pain and myalgia usually preceded serum CK elevation. Among patients with Grade 2 or higher CK elevations, the median time to onset was 12.9 weeks (range: 2 to 39 weeks) and the median time to resolution (to ≤ Grade 1) was 12 days (95% CI: 8 to 14 days). ODOMZO was temporarily interrupted in 8% of patients or permanently discontinued in 8% of patients for musculoskeletal adverse reactions. The incidence of musculoskeletal adverse reactions requiring medical intervention (magnesium supplementation, muscle relaxants, and analgesics or narcotics) was 29%, including four patients (5%) who received intravenous hydration or were hospitalized.

Obtain baseline serum CK and creatinine levels prior to initiating ODOMZO, periodically during treatment, and as clinically indicated (e.g., if muscle symptoms are reported). Obtain serum creatinine and CK levels at least weekly in patients with musculoskeletal adverse reactions with concurrent serum CK elevation greater than 2.5 times ULN until resolution of clinical signs and symptoms. Depending on the severity of symptoms, temporary dose interruption or discontinuation may be required for musculoskeletal adverse reactions or serum CK elevation [see *Dosage and Administration* (2.2)]. Advise patients starting therapy with ODOMZO of the risk of muscle-related adverse reactions. Advise patients to report promptly any new unexplained muscle pain, tenderness or weakness occurring during treatment or that persists after discontinuing ODOMZO.

5.3 Premature Fusion of the Epiphyses

Premature fusion of the epiphyses has been reported in pediatric patients exposed to ODOMZO and other Hh pathway inhibitors. Despite discontinuation of drug, cases of progressive of epiphyseal fusion have been reported in pediatric patients receiving other Hh pathway inhibitors. ODOMZO is not indicated for use in pediatric patients.

6 ADVERSE REACTIONS

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

- Musculoskeletal Adverse Reactions [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 clinical practice.

The safety of ODOMZO was evaluated in BOLT, a randomized, double-blind, multiple cohort trial in which 229 patients received ODOMZO at either 200 mg (n=79) or 800 mg (n=150) daily. The frequency of common adverse reactions including muscle spasms, alopecia, dysgeusia, fatigue, nausea, decreased weight, decreased appetite, myalgia, pain, and vomiting was greater in patients treated with ODOMZO 800 mg as compared to 200 mg.

The data described below reflect exposure to ODOMZO 200 mg daily in 79 patients with locally advanced BCC (laBCC; n=66) or metastatic BCC (mBCC; n=13) enrolled in BOLT. Patients were followed for at least 18 months unless discontinued earlier. The median duration of treatment with ODOMZO was 11.0 months (range 1.3 to 33.5 months).

The study population characteristics were: median age of 67 years (range 25 to 92; 59% were ≥65 years), 61% male, and 90% white. The majority of patients had prior surgery (75%), radiotherapy (24%), systemic chemotherapy (4%), or topical or photodynamic therapies (18%) for treatment of BCC. No patient had prior exposure to a Hh pathway inhibitor.

ODOMZO was permanently discontinued in 34% of patients or temporarily interrupted in 20% of patients for adverse reactions. Adverse reactions reported in at least two patients that led to discontinuation of the drug were: muscle spasms, and dysgeusia (each 5%), asthenia, increased lipase, and nausea (each 4%), fatigue, decreased appetite, alopecia, and decreased weight (each 3%). Serious adverse reactions occurred in 18% of patients.

The most common adverse reactions occurring in ≥10% of patients treated with ODOMZO 200 mg were muscle spasms, alopecia, dysgeusia, fatigue, nausea, musculoskeletal pain, diarrhea, decreased weight, decreased appetite, myalgia, abdominal pain, headache, pain, vomiting, and pruritus (Table 1).

The key laboratory abnormalities are described in Table 2.

Table 1: Adverse Reactions Occurring in ≥10% of Patients in BOLT

Adverse Reaction	ODOMZO 200 mg (N=79)	
	All Grades ^a %	Grade 3 %
Musculoskeletal and connective tissue		
Muscle spasms	54	3
Musculoskeletal pain	32	1
Myalgia	19	0
Skin and subcutaneous tissue		
Alopecia	53	0
Pruritus	10	0
Nervous system		
Dysgeusia	46	0
Headache	15	1
General		
Fatigue	41	4
Pain	14	1
Gastrointestinal		
Nausea	39	1
Diarrhea	32	1
Abdominal pain	18	0
Vomiting	11	1
Investigations		
Decreased weight	30	3
Metabolism and nutrition		
Decreased appetite	23	1

^a No Grade 4 adverse reactions were reported.

Table 2: Key Laboratory Abnormalities^a in BOLT

Laboratory Test	ODOMZO 200 mg (N=79)	
	All Grades %	Grades 3-4 %
Chemistry		
Increased serum creatinine	92 ^b	0
Increased serum creatine kinase (CK)	61	8
Hyperglycemia	51	4
Increased lipase	43	13
Increased alanine aminotransferase	19	4
Increased aspartate aminotransferase	19	4
Increased amylase	16	1
Hematology		
Anemia	32	0
Lymphopenia	28	3

^a Based on worst post-treatment laboratory value regardless of baseline; grading by CTCAE v4.03.

^b The serum creatinine level remained within normal range in 76% (60/79) of patients.

Amenorrhea

Amenorrhea lasting for at least 18 months occurred in two of 14 pre-menopausal women treated with ODOMZO 200 mg or 800 mg once daily.

7 DRUG INTERACTIONS

7.1 Effects of Other Drugs on ODOMZO

Strong and Moderate CYP3A Inhibitors

Avoid concomitant administration of ODOMZO with strong CYP3A inhibitors [see *Clinical Pharmacology* (12.3)].

Avoid concomitant administration of ODOMZO with moderate CYP3A inhibitors. If a moderate CYP3A inhibitor must be used, administer the moderate CYP3A inhibitor for less than 14 days and monitor closely for adverse reactions particularly musculoskeletal adverse reactions [see *Clinical Pharmacology* (12.3)].

Strong and Moderate CYP3A Inducers

Avoid concomitant administration of ODOMZO with strong and moderate CYP3A inducers [see *Clinical Pharmacology* (12.3)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on its mechanism of action and data from animal reproduction studies, ODOMZO can cause fetal harm when administered to a pregnant woman [see *Clinical Pharmacology* (12.1)]. There are no available data on the use of ODOMZO in pregnant women. In animal reproduction studies, oral administration of sonidegib during organogenesis at doses below the recommended human dose of 200 mg resulted in embryotoxicity, fetotoxicity, and teratogenicity in rabbits (see Data). Teratogenic effects observed included severe midline defects, missing digits, and other irreversible malformations. Advise pregnant women of the potential risk to a fetus. Report pregnancies to Sun Pharmaceutical Industries, Inc. at 1-800-406-7984.

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

Data

Animal Data

Daily oral administration of sonidegib to pregnant rabbits resulted in abortion, complete resorption of fetuses, or severe malformations at ≥ 5 mg/kg/day (approximately 0.05 times the recommended human dose based on AUC). Teratogenic effects included vertebral, distal limb and digit malformations, severe craniofacial malformations, and other severe midline defects. Skeletal variations were observed when maternal exposure to sonidegib was below the limit of detection.

8.2 Lactation

No data are available regarding the presence of sonidegib in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Because of the potential for serious adverse reactions in breastfed infants, advise women not to breastfeed during treatment with ODOMZO and for 20 months after the last dose.

8.3 Females and Males of Reproductive Potential

Based on its mechanism of action and animal data, ODOMZO can cause fetal harm when administered to a pregnant woman [see *Use in Specific Populations* (8.1)].

Pregnancy Testing

Verify the pregnancy status of females of reproductive potential prior to initiating ODOMZO treatment.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with ODOMZO and for at least 20 months after the last dose.

Males

It is not known if sonidegib is present in semen. Advise male patients to use condoms, even after a vasectomy, to avoid potential drug exposure to pregnant partners and female partners of reproductive potential during treatment with ODOMZO and for at least 8 months after the last dose.

Advise males not to donate semen during treatment with ODOMZO and for at least 8 months after the last dose.

Infertility

Based on findings from animal studies, female fertility may be compromised with ODOMZO [see *Nonclinical Toxicology* (13.1)].

8.4 Pediatric Use

The safety and effectiveness of ODOMZO have not been established in pediatric patients.

Epiphyseal disorders, including premature fusion of the epiphyses, have been reported in pediatric patients exposed to ODOMZO in a clinical trial. In some cases, pediatric patients treated with other Hh pathway inhibitors have experienced progression of epiphyseal fusion despite discontinuation of the Hh pathway inhibitor.

Juvenile Animal Data

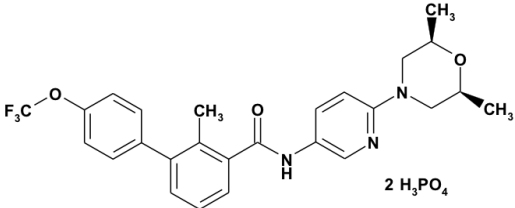
In a 5-week juvenile rat toxicology study, effects of sonidegib were observed in bone, teeth, reproductive tissues, and nerves at doses ≥10 mg/kg/day (approximately 1.2 times the recommended human dose based on AUC). Bone findings included thinning/closure of bone growth plate, decreased bone length and width, and hyperostosis. Findings in teeth included missing or fractured teeth, and atrophy. Reproductive tissue toxicity was evidenced by atrophy of testes, ovaries, and uterus, partial development of the prostate gland and seminal vesicles, and inflammation and aspermia of the epididymis. Nerve degeneration was also noted.

8.5 Geriatric Use

Of the 229 patients who received ODOMZO (79 patients receiving 200 mg daily and 150 patients receiving 800 mg daily) in BOLT, 54% were 65 years and older, while 28% were 75 years and older. No overall differences in effectiveness were observed between these patients and younger patients. There was a higher incidence of serious adverse reactions, Grade 3 and 4 adverse reactions, and adverse reactions requiring dose interruption or discontinuation in patients ≥65 years compared with younger patients; this was not attributable to an increase in any specific adverse event.

11 DESCRIPTION

Sonidegib is a Hh pathway inhibitor. The molecular formula for sonidegib phosphate is C₂₆H₂₆F₃N₃O₇·2H₃PO₄. The molecular weight is 681.49 daltons. The chemical name is N-[6-(cis-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy) [1,1'-biphenyl]-3-carboxamide diphosphate. The molecular structure is shown below:



Sonidegib phosphate is a white to off-white powder. Sonidegib freebase is practically insoluble.

ODOMZO (sonidegib) capsules for oral use contain 200 mg of sonidegib as the freebase (equivalent to 281 mg of diphosphate salt of sonidegib) and the following inactive ingredients: colloidal silicon dioxide, crospovidone, lactose monohydrate, magnesium stearate, poloxamer and sodium lauryl sulfate. The opaque pink hard gelatin capsule shell contains gelatin, red iron oxide, and titanium dioxide. The black printing ink contains ammonium hydroxide, black iron oxide, propylene glycol, and shellac.

