

ODOMZO (sonidegib) 200 mg capsules

Black box warning for embryotoxic, fetotoxic and teratogenic effects

Mechanism of action: hedgehog inhibitor that works on the transmembrane protein SMO to inhibit the HH pathway

Dosage: **200 mg po once daily** taken on an empty stomach, at least **1 hour before or 2 hours after** a meal

Lab: Obtain **serum creatine kinase (CK)** (60-70%) and **creatinine** (92%) levels prior to initiating therapy

Pharmacokinetics:

1. Half-life ($T_{1/2}$) = **28** days
2. Steady state reached at **4** months
3. Odomzo and its metabolites are eliminated primarily by the **hepatic** route

Common **Adverse Events**:

1. Muscle Spasms 54%, musculoskeletal pain 32%, myalgia 19%
2. Alopecia 53%
3. Taste disturbances (dysgeusia) 46%
4. Fatigue 41%, pain 14%
5. Nausea 39%, diarrhea 32%, abdominal pain 18%, vomiting 11%
6. Decreased weight 30%, decreased appetite 23%

Drug Interactions:

Acid reducing agents (proton pump inhibitors, antacids) do **NOT** meaningfully reduce exposure to **ODOMZO**

In vitro studies suggest that ODOMZO does **NOT** inhibit BCRP

CYP3A inhibitors can **increase** the concentration of ODOMZO (sonidegib)

Antifungal Agents:	Antibiotics	Antivirals	Calcium Channel Blockers	GI	Other
Ketoconazole (Nizoral)	Clarithromycin (Biaxin, Klaricid)	Ritonavir (Norvir)	Diltiazem (Cardiazem)	Cimetidine (Tagamet)	Grapefruit Juice
Itraconazole (Sporanox)	Erythromycin	Indinavir (Crixivan)	Verapamil (Calan, Isoptin, Verelan)		Amiodarone (Cordarone, Pacerone)
Fluconazole (Diflucan) (at high doses)	Telithromycin (Ketek)	Nelfinavir (Viracept)			Aprepitant (Emend)
Voriconazole		Saquinavir (Inverase, Fortovase)			Cyclosporine (Sandimmune, Neoral)
		Cobicistat (Tybost)			Nefazodone (Serzone)



CYP3A inducers can **decrease** the concentration of ODOMZO (sonidegib)

Antiepileptic drugs	Antituberculosis drugs	HIV Meds	Glucocorticoids	Herbal	Other
Carbamazepine (Tegretol)	Rifampin (Rifadine)	Efavirenz (Sustiva)	Dexamethasone	St. Johns Wort (Hypericum perforatum)	Modafinil (Provigil)
Phenytoin (Dilantin)	Rifabutin (Mycobutin)	Nevirapine (Viramune)	Prednisone		
Phenobarbital (Luminal)					



Both **statins** and HHI, like ODOMZO, are metabolized by CYP3A4. When used concurrently, they may compete for the same metabolic pathway, potentially leading to increased plasma concentrations of one or both drugs. Regular monitoring of liver enzymes and muscle symptoms is advised. Using a statin that is not primarily metabolized by CYP3A4, such as pravastatin (Pravachol) or rosuvastatin (Crestor) might be preferred.

L-Carnitine Prevents Muscle Cramps associated with Hedgehog Pathway Inhibitors

L-Carnitine: a naturally occurring amino acid derivative that plays a crucial role in energy production by transporting long-chain fatty acids into the mitochondria for oxidation. By enhancing energy supply to muscles, these cells can more readily pump out the calcium that has flooded the cell because of HHI usage.

Dosage: **1000-2000 mg per day**

L-carnitine is excreted by the **kidneys** (do not use in those with significantly impaired renal function)

Mild to moderate drug interactions can occur with **warfarin** (L-carnitine may have very mild anticoagulant activity) and possibly with **thyroid medications** (may make thyroid replacement therapy less effective).