

Sonidegib Therapeutic Cheat Sheet

COMPILED BY: NAGASAI C. ADUSUMILLI, MD, MBA; REVIEWED BY: ADAM J. FRIEDMAN, MD, FAAD

TRADE NAME¹

- > Odomzo

MECHANISM OF ACTION

- > Smoothed (SMO) antagonist in the Hedgehog signaling pathway,¹ summarized below
- > SMO starts cascade of interacting proteins that culminate in GLI transcription factors altering repair of DNA damage²
- > Patched 1 (PTCH1) normally inhibits SMO²
- > Activating mutations in SMO and loss of function mutations in PTCH1, identified in sporadic basal cell carcinomas (BCC) and in nevoid BCC syndrome, lead to uncontrolled abnormal DNA repair.²

FDA APPROVED FOR¹

- > Adult patients with recurrence of locally advanced basal cell carcinoma (laBCC) after surgery or radiation
- > Adult patients with laBCC not amenable to surgery or radiation

OFF-LABEL DERMATOLOGIC USES

- > Nevoid BCC syndrome (previously Gorlin syndrome)³
- > Xeroderma pigmentosum – reported only with vismodegib⁴

ADULT ORAL DOSING¹

- > 200 mg daily

ADMINISTRATION CONSIDERATIONS

- > Should take orally on an empty stomach,¹ to minimize unwanted systemic exposure with a high-fat meal
- > Concomitant amlodipine 10mg daily may reduce frequency of muscle spasms⁵
- > Various alternate dosing regimens to mitigate the severity of side effects have been reported through retrospective analyses, with reasonable clinical responses
 - > Every other day⁶
 - > Every 3rd or 4th day⁷
 - > “Drug holiday” with 1-4 months of no doses⁸

SIDE EFFECTS

- > Most common (54%): muscle spasms (specifically of lower extremities at night), myalgias^{9,10}
- > Hair loss (49%), taste changes (44%)^{9,10}
- > Decreased appetite and weight secondary to dysgeusia⁹
- > Diarrhea, headache, pruritus⁹
- > Longer time to onset, less frequency, and less severity of above side effects when compared to vismodegib¹⁰

DRUG INTERACTIONS¹

- > Avoid concomitant use with moderate and strong CYP3A inhibitors, such as itraconazole, voriconazole, fluconazole, nefazodone, diltiazem, and saquinavir.
- > Avoid concomitant use with moderate and strong CYP3A inducers, such as carbamazepine, phenobarbital, phenytoin, rifampin, rifabutin, efavirenz, and St. John’s Wort.

CONTRAINDICATIONS

- > No absolute contraindications¹
- > Discontinue if creatinine kinase (CK) elevation >2.5x upper limit of normal (ULN) with worsening renal function¹
- > Discontinue if CK elevation >10x ULN¹
- > Discontinue if CK elevation >5x ULN (recurrent)¹
- > To date, cases of laBCC refractory to vismodegib have NOT responded better to sonidegib¹¹

PREGNANCY & BREASTFEEDING¹

- > Embryotoxic, fetotoxic, and teratogenic in rabbit models at less than the 200 mg dose.
- > Patients of reproductive potential: recommend effective contraception during treatment + at least 20 months after last dose.
- > Patients with partners of reproductive potential: recommend barrier contraception during treatment + at least 8 months after last dose.
- > Avoid breastfeeding during treatment + at least 20 months after last dose
- > Avoid blood product donation during treatment + at least 20 months after last dose to avoid risk of exposure to someone of reproductive potential
- > Report any pregnancies within these parameters to Sun Pharmaceutical Industries, Inc. at 1-800-406-7984.

MONITORING¹

- > Baseline Labs:
 - > b-HCG if with reproductive potential, kidney function, CK
 - > Hep B screening per American Society of Clinical Oncology¹²
- > Periodic monitoring:
 - > Repeat CK and kidney function if severe muscle spasms or myalgias
 - > Weekly CK and kidney function if CK >2.5x ULN, until resolution

REFERENCES

1. ODOMZO [prescribing information]. Sun Pharmaceuticals Industries, Inc.; Revised Sept 2017. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/205266s0041bl.pdf. Accessed April 27, 2024.
2. Epstein EH. Basal cell carcinomas: attack of the hedgehog. *Nat Rev Cancer*. 2008 Oct;8(10):743-54. PMID: 18813320.
3. Lear JT, Hauschild A, Stockfleth E, et al. Efficacy and safety of sonidegib in adult patients with nevoid basal cell carcinoma syndrome (Gorlin syndrome): results from a phase 2, double-blind, randomized trial. *Clin Cosmet Investig Dermatol*. 2020 Feb 3;13:117-121. PMID: 32104037.
4. Soura E, Plaka M, Dessinioti C, et al. Use of vismodegib for the treatment of multiple basal cell carcinomas in a patient with xeroderma pigmentosum. *Pediatr Dermatol*. 2018 Nov;35(6):e334-e336. PMID: 30178564.
5. Ally MS, Tang JY, Lindgren J, et al. Effect of calcium channel blockade on vismodegib-induced muscle cramps. *JAMA Dermatol*. 2015 Oct;151(10):1132-4. PMID: 26200175.
6. Villani A, Costa C, Fabbrocini G, Ruggiero A, Scalvenzi M. Dose reduction during routine treatment of locally advanced basal cell carcinoma with the hedgehog inhibitor sonidegib to manage adverse effects: A retrospective case series. *J Am Acad Dermatol*. 2021 Apr;84(4):e211-e212. PMID: 33301802.
7. Woltsche N, Pichler N, Wolf I, Di Meo N, Zalaudek I. Managing adverse effects by dose reduction during routine treatment of locally advanced basal cell carcinoma with the hedgehog inhibitor vismodegib: a single centre experience. *J Eur Acad Dermatol Venereol*. 2019 Apr;33(4):e144-e145. PMID: 30472793.
8. Scalvenzi M, Costa C, Cappello M, Villani A. Reply to Woltsche N. et al. Managing adverse effects by dose reduction during routine treatment of locally advanced basal cell carcinoma with the hedgehog inhibitor vismodegib: a single-centre experience. *J Eur Acad Dermatol Venereol*. 2019 Apr;33(4):e145-e147. PMID: 30720897.
9. Dummer R, Guminski A, Gutzmer R, et al. Long-term efficacy and safety of sonidegib in patients with advanced basal cell carcinoma: 42-month analysis of the phase II randomized, double-blind BOLT study. *Br J Dermatol*. 2020 Jun;182(6):1369-1378. PMID: 31545507.
10. Dummer R, Ascierto PA, Basset-Seguín N, et al. Sonidegib and vismodegib in the treatment of patients with locally advanced basal cell carcinoma: a joint expert opinion. *J Eur Acad Dermatol Venereol*. 2020 Sep;34(9):1944-1956. PMID: 31990414.
11. Danial C, Sarin KY, Oro AE, Chang AL. An investigator-initiated open-label trial of sonidegib in advanced basal cell carcinoma patients resistant to vismodegib. *Clin Cancer Res*. 2016 Mar 15;22(6):1325-9. PMID: 26546616.
12. Hwang JP, Feld JJ, Hammond SP, et al. Hepatitis B virus screening and management for patients with cancer prior to therapy: ASCO provisional clinical opinion update. *J Clin Oncol*. 2020 Nov 1;38(31):3698-3715. PMID: 32716741.